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Serial Number: 08/983,474 Results Format Preferred (circle): PAPER DISK E-MAIL

Title of Invention Alpha-Beta C4BP-Type Recombinant Heterotrimeric Protein

Inventors (please provide full names): David Klatzmann & Jacques Cohen

Earliest Priority Date: 6/30/1998

Keywords (include any known synonyms registry numbers, explanation of initialisms):

**Search Topic:**

Please write detailed statement of the search topic, and the concept of the invention. Describe as specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. You may include a copy of the abstract and the broadcast or most relevant claim(s).

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*  U.S. PATENT TEXT FILE *
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=> e klatzman, david/in

| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 1 | KLATZKA, JOSEPH H/IN |
| E2 | USPAT | 1 | KLATZKOW, LEIF/IN |
| E3 | USPAT | 0 | --> KLATZMAN, DAVID/IN |
| E4 | USPAT | 2 | KLATZMANN, DAVID/IN |
| E5 | USPAT | 1 | KLAUBA, BRUCE/IN |
| E6 | USPAT | 4 | KLAUBER, GERALD/IN |
| E7 | USPAT | 1 | KLAUBER, MARK/IN |
| E8 | USPAT | 16 | KLAUBER, ROBERT D/IN |
| E9 | USPAT | 2 | KLAUBERT, DIETER/IN |
| E10 | USPAT | 22 | KLAUBERT, DIETER H/IN |
| E11 | USPAT | 2 | KLAUBERT, EARL C/IN |
| E12 | USPAT | 3 | KLAUCIC, LUCIANO/IN |

=> s e4

L1 2 "KLATZMANN, DAVID"/IN

=> d l1 cit ab 1-2

1. 5,843,432, Dec. 1, 1998, Retroviral vectors for the treatment of tumors, and cell lines containing them; **David Klatzmann**, et al., 424/93.21; 435/69.1, 320.1, 325 [IMAGE AVAILABLE]

US PAT NO: 5,843,432 [IMAGE AVAILABLE] L1: 1 of 2

ABSTRACT:

The invention relates to recombinant retroviral vectors, derived from Moloney MuLV, carrying a suicide gene susceptible of transforming an inactive substance into a toxic substance for cells going through a division process, said vectors being characterized by the presence in their structure of LTR sequences from variants of MuLV, and having the properties: (a) of not being inactivated during passage through the carcino-embryonic or line germinal cells of mice; (b) the expression of the suicide gene kills only the cells in the course of division.

2. 5,514,542, May 7, 1996, Methods for propagating retrovirus for use in antibody assays; Robert C. Nowinski, et al., 435/5, 7.1, 7.2, 7.9, 7.92, 235.1, 239, 974 [IMAGE AVAILABLE]

US PAT NO: 5,514,542 [IMAGE AVAILABLE] L1: 2 of 2

ABSTRACT:
Cell lines which lack human class II histocompatibility antigens are disclosed. The cell lines may be utilized within a method for propagating microorganisms, such as viruses, for determining the presence and/or amount of antibody to a microorganism in a biological fluid, and within a method for producing antibodies to a selected microorganism.

=> e coen, jacques/in

| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 1 | COEN, ERNESTO/IN |
| E2 | USPAT | 2 | COEN, GUNTHER/IN |
| E3 | USPAT | 0 | --> COEN, JACQUES/IN |
| E4 | USPAT | 2 | COEN, MANUS/IN |
| E5 | USPAT | 1 | COEN, ROBERT/IN |
| E6 | USPAT | 2 | COEN, THOMAS P/IN |
| E7 | USPAT | 1 | COEN, THOMAS T/IN |
| E8 | USPAT | 1 | COENAN, MICHEL J W/IN |
| E9 | USPAT | 2 | COENDERS, JOHANNES W/IN |
| E10 | USPAT | 3 | COENDERS, JOHANNES WILHELMUS/IN |
| E11 | USPAT | 2 | COENDERS, WILLI/IN |
| E12 | USPAT | 1 | COENDOZ, JEAN PIERRE/IN |

=> e cohen, jacques/in

| E# | FILE | FREQUENCY | TERM |
|---|---|---|---|
| E1 | USPAT | 2 | COHEN, JACOB/IN |
| E2 | USPAT | 5 | COHEN, JACOB I/IN |
| E3 | USPAT | 9 | --> COHEN, JACQUES/IN |
| E4 | USPAT | 6 | COHEN, JAMES/IN |
| E5 | USPAT | 2 | COHEN, JAMES A/IN |
| E6 | USPAT | 2 | COHEN, JAMES D/IN |
| E7 | USPAT | 2 | COHEN, JASON M/IN |
| E8 | USPAT | 1 | COHEN, JAY B/IN |
| E9 | USPAT | 1 | COHEN, JEAN PIERRE D/IN |
| E10 | USPAT | 1 | COHEN, JEANNIE/IN |
| E11 | USPAT | 1 | COHEN, JEFFERY M/IN |
| E12 | USPAT | 5 | COHEN, JEFFREY/IN |

=> s e3

L2 9 "COHEN, JACQUES"/IN

=> d l2 cit ab 1-9

1. 5,415,155, May 16, 1995, Modular element with multiple conduits; **Jacques Cohen**, et al., 126/663; 138/111, 115, 155 [IMAGE AVAILABLE]

US PAT NO: 5,415,155 [IMAGE AVAILABLE] L2: 1 of 9

ABSTRACT:
This modular element has several conduits disposed side by side, each pair of adjacent conduits being interconnected to form a rigid or flexible unit, each conduit has a male end and an opposite female end, the latter for joining with the male end of an aligned conduit of an adjacent modular element. The several conduits of a first modular element can therefore be simultaneously extended by the several conduits of a second modular element by simultaneously joining the female and male ends of the elements. These elements can be in the form of panels to be joined together to form, for instance, a solar panel or a floor covering with a circulating heat transfer fluid through the conduits. The conduits may also serve as protected passages for underground electrical wires. The conduits may be provided with sprinkler holes to water plants. The panels preferably have interlocking means on their sides which are parallel to the conduits for interlocking adjacent panels and these sides may be provided with fastening zones to fasten the panels to an underlying surface. The panels can be fitted with a transparent cover enclosing an air chamber allowing sun rays therethrough but preventing heat escape when used as solar panels.

2. 5,144,530, Sep. 1, 1992, Power distributor device for electric installations; **Jacques Cohen**, et al., 361/675; 174/99B; 361/638, 649; 439/114, 213, 714, 949 [IMAGE AVAILABLE]

US PAT NO: 5,144,530 [IMAGE AVAILABLE] L2: 2 of 9

ABSTRACT:
A power distributor device is disclosed for electric installations, comprising, for housing a set of power bars, an insulating case formed preferably of several interlockable modules. A member, for example an end-piece in the form of a lyre is associated with a zone for fixing the case on a support allowing expansion between the case and the support. An upstream connection box may be assembled to the case and comprise a zone for fixing to the support.

3. 4,855,698, Aug. 8, 1989, Protective switching apparatus with remotely controlled opening and closing of the contacts; **Jacques Cohen**, et al., 335/14, 20 [IMAGE AVAILABLE]

US PAT NO: 4,855,698 [IMAGE AVAILABLE] L2: 3 of 9

ABSTRACT:
A protective switching apparatus with remote controlled opening and closing is provided including a tripping mechanism connected to an assembly comprising at least two fixed contacts and two mobile contacts and to a magnetic and/or thermal trip; a resetting member and an electromagnet having a movable element and to a member for driving a least one pseudo-fixed or mobile contact. The mobile contacts are carried by a bridge having a plane of symmetry X--X and the tripping mechanism extends in the vicinity of the plane of symmetry X--X. The electromagnet and the trip are housed in the case on each side of the tripping mechanism in a direction perpendicular to the plane of symmetry.

4. 4,650,937, Mar. 17, 1987, Automatic protection switch with visible disconnecting action and manual resetting; Elie Belbel, et al., 200/434, 50.17, 50.21, 61.19, 573 [IMAGE AVAILABLE]

US PAT NO: 4,650,937 [IMAGE AVAILABLE] L2: 4 of 9

ABSTRACT:

An electric switch apparatus for protecting an electric circuit, said apparatus comprising a case, a pivoting drawer connected to the case and adapted to be manually pivoted from a closed position to an open position and reversely, a switch having a fixed and a movable contact, the movable contact being mechanically linked to the drawer for simultaneous opening therewith and a breaking member for automatically breaking an electric circuit connected across two terminals of the case, the said breaking member operating in case of an overflow of current in the said circuit, the movable contact being able to be separated from the fixed contact under the action of an actuation member comprising a spring and a magnetizable member, said actuating member cooperating with a coil placed in the circuit and being reset during a manual opening and closing movement of the drawer.

5. D 263,518, Mar. 30, 1982, Sole for footwear; **Jacques Cohen**, D2/954 [IMAGE AVAILABLE]

US PAT NO: D 263,518 [IMAGE AVAILABLE] L2: 5 of 9

6. D 263,348, Mar. 16, 1982, Sole for footwear; **Jacques Cohen**, D2/954 [IMAGE AVAILABLE]

US PAT NO: D 263,348 [IMAGE AVAILABLE] L2: 6 of 9

7. 4,296,396, Oct. 20, 1981, Manual electric switch with thermal release; Raymond A. Ingrain, et al., 337/66, 58, 70 [IMAGE AVAILABLE]

US PAT NO: 4,296,396 [IMAGE AVAILABLE] L2: 7 of 9

ABSTRACT:
In a manual switch with thermal and magnetic release, the fixed pivots of a control member, of a latch, and of a transmission member coupled to the contacts, are disposed at the apices of a right-angled triangle, one side bounding the right angle being parallel to the direction of actuation of the control member and to the movement of the contacts, the other side bounding the right angle being placed in the vicinity of the control member.

8. 4,223,456, Sep. 23, 1980, Shoe sole assembly; **Jacques Cohen**, 36/29, 3B, 32R, 59R [IMAGE AVAILABLE]

US PAT NO: 4,223,456 [IMAGE AVAILABLE] L2: 8 of 9

ABSTRACT:
A shoe sole assembly of a resilient material body portion provided with absorbers energy formed as part of the body portion. The energy absorbers are defined by vertically disposed, spaced apart cell members extending from an upper surface to beyond a lower surface of the body portion to provide a bounded space. Each cell member is formed of an hollow compartment extending in part for the thickness of the body portion with its length depending upon the sole profile, the first end of the respective compartments at the upper surface of the sole body portion is initially open ended; whereas a hollow protuberance structure is at the lower surface of the body portion to enclose each cylindrical compartment at a second end. The protuberances extend beyond the lower surface to form contact areas with the ground surface when the sole assembly is used as part of a shoe. The compartments are separated from one another by adjacent lands which at the upper sole surface provide define respective substrate areas for the disposition of an inner sole thereon, so to seal each cell member with a volume of air trapped in the bounded space of the compartment and associated hollow protuberance structure.

9. 3,839,691, Oct. 1, 1974, SETTING AND TRIGGERING DEVICE FOR THERMAL RELAY; **Jacques Cohen**, et al., 337/132, 66, 72 [IMAGE AVAILABLE]

US PAT NO: 3,839,691 [IMAGE AVAILABLE] L2: 9 of 9

ABSTRACT:
A thermal relay designed to control the power supply circuit of a contactor, said thermal relay comprising movable contacts cooperating with stationary contacts, a triggering slide released by thermoelements for displacing the movable contacts to open the circuit in case of excessive current flow and a hand control, controlling the slide and the movable contacts for opening or closing the circuit. The slide cannot be reset in proper position for closing the circuits unless the thermoelements are cold.

=> s c4bp

L3 44 C4BP

=> s c4bp?

L4 44 C4BP?

=> s l4 and (cd4 or cd8 or cd16 or cd35 or cr1)

2956 CD4
1390 CD8
237 CD16
28 CD35
3679 CR1
L5 22 L4 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1)

=> s l5 and scfv?

112 SCFV?
L6 0 L5 AND SCFV?

=> s l5 and erythrocyte?

6907 ERYTHROCYTE?
L7 14 L5 AND ERYTHROCYTE?

=> s l7 and (alpha or beta)

270378 ALPHA
181872 BETA
L8 14 L7 AND (ALPHA OR BETA)

=> d l8 cit ab 1-14

1. 5,869,615, Feb. 9, 1999, Modified complement proteases; Dennis E.
Hourcade, et al., 530/380; 435/69.1; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,869,615 [IMAGE AVAILABLE] L8: 1 of 14

ABSTRACT:
Variant complement proteins that are modified in their complement-mediated activity are provided, along with methods for their preparation, and their potential uses. The modifications comprise amino acid substitutions in regions of the complement proteins that contain certain motifs also present in homologous proteins. The amino acid substitutions and their effect on the complement activity of the modified protein are also provided.

2. 5,863,542, Jan. 26, 1999, Recombinant attenuated ALVAC canaryopox virus containing heterologous HIV or SIV inserts; Enzo Paoletti, et al., 424/199.1, 188.1, 208.1, 232.1; 435/236 [IMAGE AVAILABLE]

US PAT NO: 5,863,542 [IMAGE AVAILABLE] L8: 2 of 14

ABSTRACT:
Attenuated recombinant viruses containing DNA encoding an immunodeficiency virus and/or CTL antigen, as well as methods and compositions employing the viruses, expression products therefrom, and antibodies generated from the viruses or expression products, are disclosed and claimed. The recombinant viruses can be NYVAC or ALVAC recombinant viruses. The DNA can code for at least one of: HIV1gag(+pro)(IIIB), gp120(MN)(+transmembrane), nef(BRU)CTL, pol(IIIB)CTL, ELDKWA or LDKW epitopes, preferably HIV1gag(+pro)(IIIB), gp120(MN) (+transmembrane), two (2) nef(BRU)CTL and three (3) pol(IIIB)CTL epitopes; or two ELDKWA in gp120 V3 or another region or in gp160. The two (2) nef(BRU)CTL and three (3) pol(IIIB)CTL epitopes are preferably CTL1, CTL2, pol1, pol2 and pol3. The recombinant viruses and gene products therefrom and antibodies generated by the viruses and gene products have several preventive, therapeutic and diagnostic uses. DNA from the recombinant viruses are useful as probes or, for generating PCR primers or for immunization. Also disclosed and claimed are HIV immunogens and modified gp160 and gp120.

3. 5,856,300, Jan. 5, 1999, Compositions comprising complement related proteins and carbohydrates, and methods for producing and using said compositions; Charles W. Rittershaus, et al., 514/12; 424/192.1, 193.1; 435/69.1, 69.6, 85; 436/501, 518; 514/8, 21; 530/395 [IMAGE AVAILABLE]

US PAT NO: 5,856,300 [IMAGE AVAILABLE] L8: 3 of 14

ABSTRACT:

The present invention provides compositions comprising at least one complement moiety and at least one carbohydrate moiety, and methods of producing such compositions. In particular, the compositions of the invention comprise complement proteins related to the complement receptor type I, and further comprise ligands for intracellular molecules, such as selectins. In a preferred embodiment, the compositions comprise a complement-related protein in combination with the Louis X antigen or the sialyl Lewis X antigen. The compositions of the invention have use in the diagnosis or therapy of disorders involving complement activity and inflammation. Pharmaceutical compositions are also provided for treating or reducing inflammation mediated by inappropriate complement activity and intercellular adhesion.

4. 5,856,297, Jan. 5, 1999, Human C3b/C4b receptor (**CR1**); Douglas T. Fearon, et al., 514/2; 435/69.1; 530/350; 536/23.4 [IMAGE AVAILABLE]

US PAT NO: 5,856,297 [IMAGE AVAILABLE] L8: 4 of 14

ABSTRACT:
Human complement receptor type 1 (**CR1**). Nucleic acid molecules encoding full-length **CR1** protein and fragments thereof having complement regulatory activity are described, as well as recombinant **CR1** protein and polypeptides, vectors for their expression, and cell lines expressing or bearing DNA molecules encoding such proteins and polypeptides, including a soluble **CR1** polypeptide consisting of the extracellular 30 short consensus repeat domains of the mature **CR1** protein. The nucleic acids and polypeptides described are useful in diagnosis and treatment of disorders involving complement activity and inflammation. Compositions useful in therapeutic applications are also disclosed.

5. 5,851,528, Dec. 22, 1998, Methods of inhibiting complement activation; Jone-Long Ko, et al., 424/185.1, 192.1; 514/12; 530/350, 380 [IMAGE AVAILABLE]

US PAT NO: 5,851,528 [IMAGE AVAILABLE] L8: 5 of 14

ABSTRACT:
The present invention relates to novel chimeric proteins comprising a first polypeptide which inhibits complement activation, linked to a second polypeptide which inhibits complement activation, nucleic acids encoding novel chimeric proteins and methods of reducing inflammation with the administration of the chimeric proteins of the invention.

6. 5,840,858, Nov. 24, 1998, Protein purification using immobilized metal affinity chromatography for complement receptor proteins; Thomas Michael Smith, et al., 530/413, 380, 395 [IMAGE AVAILABLE]

US PAT NO: 5,840,858 [IMAGE AVAILABLE] L8: 6 of 14

ABSTRACT:

This invention relates to the application of immobilized metal affinity chromatography to the purification of complement receptor proteins.

7. 5,833,975, Nov. 10, 1998, Canarypox virus expressing cytokine and/or tumor-associated antigen DNA sequence; Enzo Paoletti, et al., 424/93.2; 435/69.3, 69.5, 69.51, 69.52, 320.1, 456 [IMAGE AVAILABLE]

US PAT NO: 5,833,975 [IMAGE AVAILABLE] L8: 7 of 14

ABSTRACT:
Attenuated vaccinia or canarypox recombinant viruses containing DNA coding for a cytokine and/or a tumor associated antigen, as well as methods and compositions employing the viruses, are disclosed and claimed. The recombinant viruses can be NYVAC or ALVAC recombinant viruses. The DNA can code for at least one of: human tumor necrosis factor; nuclear phosphoprotein p53, wildtype or mutant; human melanoma-associated antigen; IL-2; IFN.gamma.; IL-4; GMCSF; IL-12; B7; erb-B-2 and carcinoembryonic antigen. The recombinant viruses and gene products therefrom are useful for cancer therapy.

8. 5,679,546, Oct. 21, 1997, Chimeric proteins which block complement activation; Jone-Long Ko, et al., 435/69.2, 69.7, 252.3, 320.1; 530/350, 412; 536/23.4 [IMAGE AVAILABLE]

US PAT NO: 5,679,546 [IMAGE AVAILABLE] L8: 8 of 1

ABSTRACT:
The present invention relates to novel chimeric proteins comprising a first polypeptide which inhibits complement activation, linked to a second polypeptide which inhibits complement activation, nucleic acids encoding novel chimeric proteins and methods of reducing inflammation with the administration of the chimeric proteins of the invention.

9. 5,514,787, May 7, 1996, DNA sequences encoding human membrane cofactor protein (MCP); John P. Atkinson, 536/23.1; 435/6, 69.1, 810; 536/24.1, 24.3, 24.31, 24.32, 24.33 [IMAGE AVAILABLE]

US PAT NO: 5,514,787 [IMAGE AVAILABLE] L8: 9 of 1

ABSTRACT:
Human membrane cofactor protein, a protein involved in regulation of complement activity, has been purified to homogeneity. The gene encoding this protein has been retrieved and permits deduction of the entire amino acid sequence and the recombinant production of this material. Pharmaceutical compositions in which MCP is the active ingredient for use in treating autoimmune diseases are also disclosed.

10. 5,472,939, Dec. 5, 1995, Method of treating complement mediated disorders; Douglas T. Fearon, et al., 514/8, 2, 12, 885, 886 [IMAGE AVAILABLE]

US PAT NO: 5,472,939 [IMAGE AVAILABLE] L8: 10 of 14

ABSTRACT:
The present invention relates to the C3b/C4b receptor (**CR1**) gene and its encoded protein. The invention also relates to **CR1** nucleic acid sequences and fragments thereof comprising 70 nucleotides and their encoded peptides or proteins comprising 24 amino acids. The invention further provides for the expression of the **CR1** protein and fragments thereof. The genes and proteins of the invention have uses in diagnosis and therapy of disorders involving complement activity, and various immune system or inflammatory disorders. In specific embodiments of the present invention detailed in the examples sections infra, the cloning, nucleotide sequence, and deduced amino acid sequence of a full-length **CR1** cDNA and fragments thereof are described. The expression of the **CR1** protein and fragments thereof is also described. Also described is the expression of a secreted **CR1** molecule lacking a transmembrane region. The secreted **CR1** molecule is shown to be useful in reducing damage caused by inflammation and in reducing myocardial infarct size and preventing reperfusion injury.

11. 5,256,642, Oct. 26, 1993, Compositions of soluble complement receptor 1 (**CR1**) and a thrombolytic agent, and the methods of use thereof; Douglas T. Fearon, et al., 514/8; 424/94.63, 94.64; 435/215, 216; 514/2; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,256,642 [IMAGE AVAILABLE] L8: 11 of 14

ABSTRACT:
The present invention relates to compositions comprising soluble complement receptor 1 (**CR1**) and a thrombolytic agent. In a specific embodiment, the thrombolytic agent is anisoylated human plasminogen-streptokinase activator complex (ASPAC). The invention further relates to methods for treating thrombotic conditions in humans and animals by administering a composition comprising soluble **CR1** and a thrombolytic agent. In particular, the compositions and methods are useful both for reducing reperfusion injury and ameliorating the other effects of myocardial infarction.

12. 5,252,216, Oct. 12, 1993, Protein purification; Gail Folena-Wasserman, et al., 210/635, 656; 530/380, 413, 416, 417, 420 [IMAGE AVAILABLE]

US PAT NO: 5,252,216 [IMAGE AVAILABLE] L8: 12 of 14

ABSTRACT:
This invention relates to the application of combination chromatography
to the purification of complement receptor proteins.

13. 5,212,071, May 18, 1993, Nucleic acids encoding a human C3b/C4b
receptor (**CR1**); Douglas T. Fearon, et al., 435/69.1, 252.3, 320.1; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,212,071 [IMAGE AVAILABLE] L8: 13 of 14

14. 4,672,044, Jun. 9, 1987, Murine monoclonal antibody combining site
to human C3b receptor (**CR1**); Robert D. Schreiber, 436/501; 435/4,
7.21, 7.24, 7.25, 70.21, 334, 810, 968, 975; 436/504, 506, 507, 512, 518, 536, 540, 548, 815, 821 [IMAGE AVAILABLE]

US PAT NO: 4,672,044 [IMAGE AVAILABLE] L8: 14 of 14

ABSTRACT:
A murine monoclonal antibody combining site produced by a hybridoma
formed by fusion of cells from a myeloma cell line and lymphocytes that
produce antibodies that react (1) with isolated human C3b receptor and
(2) with C3b receptor-bearing cells from a mammal immunized with human
C3b receptor is disclosed.

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(FILE 'USPAT' ENTERED AT 16:05:08 ON 25 APR 1999)
E KLATZMAN, DAVID/IN
L1 2 S E4
E COEN, JACQUES/IN
E COHEN, JACQUES/IN
L2 9 S E3
L3 44 S C4BP
L4 44 S C4BP?
L5 22 S L4 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1)
L6 0 S L5 AND SCFV?
L7 14 S L5 AND ERYTHROCYTE?
L8 14 S L7 AND (ALPHA OR BETA)

=> d l4 cit 1-44

1. 5,869,615, Feb. 9, 1999, Modified complement proteases; Dennis E.
Hourcade, et al., 530/380; 435/69.1; 530/350 [IMAGE AVAILABLE]

2. 5,863,542, Jan. 26, 1999, Recombinant attenuated ALVAC canaryopox
virus containing heterologous HIV or SIV inserts; Enzo Paoletti, et al.,
424/199.1, 188.1, 208.1, 232.1; 435/236 [IMAGE AVAILABLE]

3. 5,858,373, Jan. 12, 1999, Recombinant poxvirus-feline infectious peritionitis virus, compositions thereof and methods for making and using
them; Enzo Paoletti, et al., 424/199.1, 186.1, 204.1, 205.1, 221.1, 235.1; 435/69.3, 236, 237; 536/23.71 [IMAGE AVAILABLE]

4. 5,856,300, Jan. 5, 1999, Compositions comprising complement related
proteins and carbohydrates, and methods for producing and using said
compositions; Charles W. Rittershaus, et al., 514/12; 424/192.1, 193.1; 435/69.1, 69.6, 85; 436/501, 518; 514/8, 21; 530/395 [IMAGE AVAILABLE]

5. 5,856,297, Jan. 5, 1999, Human C3b/C4b receptor (CR1); Douglas T.
Fearon, et al., 514/2; 435/69.1; 530/350; 536/23.4 [IMAGE AVAILABLE]

6. 5,851,528, Dec. 22, 1998, Methods of inhibiting complement activation; Jone-Long Ko, et al., 424/185.1, 192.1; 514/12; 530/350, 380
[IMAGE AVAILABLE]

7. 5,849,585, Dec. 15, 1998, Isolating and culturing Schwann cells; Jennie P. Mather, et al., 435/368, 325, 363, 366, 384, 387, 389 [IMAGE
AVAILABLE]

8. 5,843,456, Dec. 1, 1998, Alvac poxvirus-rabies compositions and combination compositions and uses; Enzo Paoletti, et al., 424/199.1, 201.1, 202.1, 204.1, 205.1, 218.1, 224.1; 435/69.3, 235.1, 252.3, 320.1; 514/2; 530/350, 826 [IMAGE AVAILABLE]

9. 5,840,858, Nov. 24, 1998, Protein purification using immobilized metal affinity chromatography for complement receptor proteins; Thomas
Michael Smith, et al., 530/413, 380, 395 [IMAGE AVAILABLE]

10. 5,833,975, Nov. 10, 1998, Canarypox virus expressing cytokine and/or
tumor-associated antigen DNA sequence; Enzo Paoletti, et al., 424/93.2;
435/69.3, 69.5, 69.51, 69.52, 320.1, 456 [IMAGE AVAILABLE]

11. 5,830,448, Nov. 3, 1998, Compositions and methods for the treatment
of tumors; Gordon A. Vehar, 424/85.2, 85.1, 85.5; 514/2; 530/351, 381 [IMAGE AVAILABLE]

12. 5,767,241, Jun. 16, 1998, Soluble form of GMP-140; Rodger P. McEver,
530/350; 435/69.1, 252.3, 254.11, 325; 530/395; 536/23.5 [IMAGE AVAILABLE]

13. 5,766,599, Jun. 16, 1998, Trova fowl pox virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 424/199.1, 232.1;
435/69.1, 69.3, 235.1, 320.1 [IMAGE AVAILABLE]

14. 5,762,938, Jun. 9, 1998, Modified recombinant vaccinia virus and expression vectors thereof; Enzo Paoletti, et al., 424/199.1, 204.1, 205.1, 232.1; 435/320.1; 536/23.72 [IMAGE AVAILABLE]

15. 5,762,921, Jun. 9, 1998, Composition and methods for the treatment
of tumors; Gordon A. Vehar, 424/85.1, 85.2, 85.5, 158.1, 198.1; 514/12;
530/350, 351, 381 [IMAGE AVAILABLE]

16. 5,756,103, May 26, 1998, Alvac canarypox virus recombinants comprising heterlogous inserts; Enzo Paoletti, et al., 424/199.1, 204.1, 206.1, 207.1, 208.1, 214.1, 232.1; 435/69.3, 173.3, 235.1, 252.3, 320.1; 530/350, 826 [IMAGE AVAILABLE]

17. 5,756,102, May 26, 1998, Poxvirus-canine distemper virus (CDV) recombinants and compositions and methods employing the recombinants;
Enzo Paoletti, et al., 424/199.1, 213.1, 232.1; 435/69.3, 235.1, 320.1 [IMAGE AVAILABLE]

18. 5,721,139, Feb. 24, 1998, Isolating and culturing schwann cells; Jennie P. Mather, et al., 435/383, 325, 363, 366, 368, 384, 387 [IMAGE
AVAILABLE]

19. 5,719,127, Feb. 17, 1998, Modified complement system regulators;
John P. Atkinson, et al., 514/12; 530/350 [IMAGE AVAILABLE]

20. 5,714,385, Feb. 3, 1998, Media for culturing schwann cells; Jennie P. Mather, et al., 435/406, 404, 405 [IMAGE AVAILABLE]

21. 5,688,920, Nov. 18, 1997, Nucleotide and amino acid sequences for
canine herpesvirus GB, GC and GD and uses therefor; Enzo Paoletti, et
al., 530/395; 424/184.1, 199.1, 229.1, 232.1; 435/69.1, 69.3, 235.1, 236, 237, 320.1; 530/350, 403 [IMAGE AVAILABLE]

22. 5,679,546, Oct. 21, 1997, Chimeric proteins which block complement
activation; Jone-Long Ko, et al., 435/69.2, 69.7, 252.3, 320.1; 530/350, 412; 536/23.4 [IMAGE AVAILABLE]

23. 5,663,142, Sep. 2, 1997, Protein S deletion variants deficient in **C4BP** binding activity, but having APC cofactor activity, compositions
and therapeutic methods; Bonno Nammen Bouma, et al., 514/12; 530/380
[IMAGE AVAILABLE]

24. 5,656,484, Aug. 12, 1997, Protein S deletion variants deficient in **C4BP** binding activity but having APC cofactor activity compositions
and therapeutic methods; Bonno Nammen Bouma, et al., 435/252.3, 320.1;
536/23.5 [IMAGE AVAILABLE]

25. 5,545,619, Aug. 13, 1996, Modified complement system regulators;
John P. Atkinson, et al., 514/12; 530/350 [IMAGE AVAILABLE]

26. 5,529,780, Jun. 25, 1996, Nucleotide and amino acid sequences of canine herpesvirus gB and gC; Enzo Paoletti, et al., 424/199.1, 184.1, 229.1, 232.1; 435/69.1, 69.3, 235.1, 236, 237, 320.1, 456; 536/23.72, 24.1 [IMAGE AVAILABLE]

27. 5,525,708, Jun. 11, 1996, Covalent dimer of kit ligand; Karl H. Nocka, et al., 530/409, 351, 399, 417 [IMAGE AVAILABLE]

28. 5,514,787, May 7, 1996, DNA sequences encoding human membrane
cofactor protein (MCP); John P. Atkinson, 536/23.1; 435/6, 69.1, 810; 536/24.1, 24.3, 24.31, 24.32, 24.33 [IMAGE AVAILABLE]

29. 5,494,807, Feb. 27, 1996, NYVAC vaccinia virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 435/69.3; 424/199.1, 204.1, 205.1, 218.1, 224.1, 227.1, 229.1, 230.1, 231.1, 232 239.1; 435/235.1, 320.1; 514/2; 530/350, 826 [IMAGE AVAILABLE]

30. 5,472,939, Dec. 5, 1995, Method of treating complement mediated
disorders; Douglas T. Fearon, et al., 514/8, 2, 12, 885, 886 [IMAGE AVAILABLE]

31. 5,405,946, Apr. 11, 1995, Recombinant protein S variants deficient
in **C4BP** binding activity, compositions and therapeutic methods; John
H. Griffin, et al., 530/380; 435/69.6; 530/830 [IMAGE AVAILABLE]

32. 5,378,464, Jan. 3, 1995, Modulation of inflammatory responses by
administration of GMP-140 or antibody to GMP-140; Rodger P. McEver,
424/143.1; 514/8 [IMAGE AVAILABLE]

33. 5,366,861, Nov. 22, 1994, Immunoassay and reagent kit used therefor;
Kenji Hosoda, et al., 435/7.1, 7.92, 7.93, 7.94, 7.95, 15, 975; 436/536 [IMAGE AVAILABLE]

34. 5,364,773, Nov. 15, 1994, Genetically engineered vaccine strain; Enzo Paoletti, et al., 435/69.1; 424/205.1, 232.1; 435/69.3, 235.1, 236 320.1, 456; 530/300, 350 [IMAGE AVAILABLE]

35. 5,321,123, Jun. 14, 1994, Protein S polypeptides and anti-peptide antibodies that inhibit protein S binding to C4B binding protein, diagnostic systems and therapeutic methods; John H. Griffin, et al., 530/300; 435/7.93; 436/501; 530/324, 325, 327, 328, 329, 830 [IMAG AVAILABLE]

36. 5,256,642, Oct. 26, 1993, Compositions of soluble complement receptor 1 (CR1) and a thrombolytic agent, and the methods of use thereof; Douglas T. Fearon, et al., 514/8; 424/94.63, 94.64; 435/215, 216; 514/2; 530/350 [IMAGE AVAILABLE]

37. 5,252,216, Oct. 12, 1993, Protein purification; Gail Folena-Wasserman, et al., 210/635, 656; 530/380, 413, 416, 417, 420 [IMAGE AVAILABLE]

38. 5,221,628, Jun. 22, 1993, Binding of aggregated immunoglobulin or
immune complexes by serum amyloid P component; Byron E. Anderson, et al.,
436/507; 435/7.1, 7.8, 975; 436/501, 509, 518, 536, 538, 808 [IMAGE AVAILABLE]

39. 5,221,616, Jun. 22, 1993, Prevention of spontaneous complement activation in mammalian biological fluids; William P. Kolb, et al., 435/18; 436/69 [IMAGE AVAILABLE]

40. 5,212,071, May 18, 1993, Nucleic acids encoding a human C3b/C4b
receptor (CR1); Douglas T. Fearon, et al., 435/69.1, 252.3, 320.1; 530/350 [IMAGE AVAILABLE]

41. 5,198,534, Mar. 30, 1993, Process for preparation of activated protein C by immobilized aprotinin chromatography; Marion Steinbuch, et
al., 530/381, 380, 413 [IMAGE AVAILABLE]

42. 5,198,424, Mar. 30, 1993, Functionally active selectin-derived peptides; Rodger P. McEver, 514/13; 424/1.37, 1.69; 427/2.24, 2.25; 514/12, 14, 15, 16; 530/324, 325, 326, 327; 623/11 [IMAGE AVAILABLE]

43. 5,187,067, Feb. 16, 1993, Immunological determination of free human
protein S and **C4bp**-protein S complex; Yukiya Koike, et al., 435/7.9,
7.1, 337; 436/821, 824; 530/387.1, 388.25, 412, 413 [IMAGE AVAILABLE]

44. 4,672,044, Jun. 9, 1987, Murine monoclonal antibody combining site
to human C3b receptor (CR1); Robert D. Schreiber, 436/501; 435/4, 7.21,
7.24, 7.25, 70.21, 334, 810, 968, 975; 436/504, 506, 507, 512, 518, 53 540, 548, 815, 821 [IMAGE AVAILABLE]

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E KLATZMAN, DAVID/IN
L1 2 S E4
E COEN, JACQUES/IN
E COHEN, JACQUES/IN
L2 9 S E3
L3 44 S C4BP
L4 44 S C4BP?
L5 22 S L4 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1
L6 0 S L5 AND SCFV?
L7 14 S L5 AND ERYTHROCYTE?
L8 14 S L7 AND (ALPHA OR BETA)

=> s l3 and (coagulation or complement)

20903 COAGULATION
42600 COMPLEMENT
L9 43 L3 AND (COAGULATION OR COMPLEMENT)

=> s l9 and (s protein or scr?)

1635834 S
70853 PROTEIN
528 S PROTEIN
(S(W)PROTEIN)
TERM 'SCR?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

=> s l9 and (s protein or scr or scrs)

1635834 S
70853 PROTEIN
528 S PROTEIN
(S(W)PROTEIN)
12768 SCR
2046 SCRS
L10 23 L9 AND (S PROTEIN OR SCR OR SCRS)

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1. 5,869,615, Feb. 9, 1999, Modified **complement** proteases; Dennis E.
Hourcade, et al., 530/380; 435/69.1; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,869,615 [IMAGE AVAILABLE] L10: 1 of 23

ABSTRACT:
Variant **complement** proteins that are modified in their **complement**-mediated activity are provided, along with methods for
their preparation, and their potential uses. The modifications comprise amino acid substitutions in regions of the **complement** proteins that
contain certain motifs also present in homologous proteins. The amino
acid substitutions and their effect on the **complement** activity of the
modified protein are also provided.

2. 5,856,300, Jan. 5, 1999, Compositions comprising **complement**
related proteins and carbohydrates, and methods for producing and using
said compositions; Charles W. Rittershaus, et al., 514/12; 424/192.1, 193.1; 435/69.1, 69.6, 85; 436/501, 518; 514/8, 21; 530/395 [IMAGE AVAILABLE]

US PAT NO: 5,856,300 [IMAGE AVAILABLE] L10: 2 of 23

ABSTRACT:

The present invention provides compositions comprising at least one **complement** moiety and at least one carbohydrate moiety, and methods
of producing such compositions. In particular, the compositions of the
invention comprise **complement** proteins related to the **complement**
receptor type I, and further comprise ligands for intracellular molecules, such as selectins. In a preferred embodiment, the compositions
comprise a **complement**-related protein in combination with the Louis X
antigen or the sialyl Lewis X antigen. The compositions of the invention
have use in the diagnosis or therapy of disorders involving **complement** activity and inflammation. Pharmaceutical compositions are
also provided for treating or reducing inflammation mediated by inappropriate **complement** activity and intercellular adhesion.

3. 5,856,297, Jan. 5, 1999, Human C3b/C4b receptor (CR1); Douglas T.
Fearon, et al., 514/2; 435/69.1; 530/350; 536/23.4 [IMAGE AVAILABLE]

US PAT NO: 5,856,297 [IMAGE AVAILABLE] L10: 3 of 23

ABSTRACT:
Human **complement** receptor type 1 (CR1). Nucleic acid molecules
encoding full-length CR1 protein and fragments thereof having **complement** regulatory activity are described, as well as recombinant
CR1 protein and polypeptides, vectors for their expression, and cell lines expressing or bearing DNA molecules encoding such proteins and
polypeptides, including a soluble CR1 polypeptide consisting of the extracellular 30 short consensus repeat domains of the mature CR1 protein. The nucleic acids and polypeptides described are useful in diagnosis and treatment of disorders involving **complement** activity
and inflammation. Compositions useful in therapeutic applications are
also disclosed.

4. 5,851,528, Dec. 22, 1998, Methods of inhibiting **complement** activation; Jone-Long Ko, et al., 424/185.1, 192.1; 514/12; 530/350, 380
[IMAGE AVAILABLE]

US PAT NO: 5,851,528 [IMAGE AVAILABLE] L10: 4 of 23

ABSTRACT:
The present invention relates to novel chimeric proteins comprising a first polypeptide which inhibits **complement** activation, linked to a
second polypeptide which inhibits **complement** activation, nucleic
acids encoding novel chimeric proteins and methods of reducing inflammation with the administration of the chimeric proteins of the invention.

5. 5,840,858, Nov. 24, 1998, Protein purification using immobilized metal affinity chromatography for **complement** receptor proteins;
Thomas Michael Smith, et al., 530/413, 380, 395 [IMAGE AVAILABLE]

US PAT NO: 5,840,858 [IMAGE AVAILABLE] L10: 5 of 23

ABSTRACT:

This invention relates to the application of immobilized metal affinity chromatography to the purification of **complement** receptor proteins.

6. 5,830,448, Nov. 3, 1998, Compositions and methods for the treatment
of tumors; Gordon A. Vehar, 424/85.2, 85.1, 85.5; 514/2; 530/351, 381 [IMAGE AVAILABLE]

US PAT NO: 5,830,448 [IMAGE AVAILABLE] L10: 6 of 23

ABSTRACT:
The invention concerns a method for inhibiting the growth and/or causing
regression of tumors by administering a therapeutically effective dose of
a procoagulant and a cytokine, preferably TNF-.beta., TNF-.alpha. and/or
IL-1. In a specific aspect, the invention concerns a method for tumor treatment by the administration of a therapeutically effective amount of
a thrombomodulin inhibitor and a cytokine. The invention also concerns
thrombomodulin inhibitors and pharmaceutical compositions used in the
course of these treatments.

7. 5,767,241, Jun. 16, 1998, Soluble form of GMP-140; Rodger P. McEver,
530/350; 435/69.1, 252.3, 254.11, 325; 530/395; 536/23.5 [IMAGE AVAILABLE]

US PAT NO: 5,767,241 [IMAGE AVAILABLE] L10: 7 of 23

ABSTRACT:
The invention is directed to a purified soluble form of human granule membrane protein 140 (GMP-140) which lacks an amino acid sequence
comprising a transmembrane domain and which is effective in inhibiting
leukocyte adherence mediated by granule membrane protein 140. Nucleic
acid encoding the soluble form of GMP-140 is disclosed.

8. 5,766,599, Jun. 16, 1998, Trova fowl pox virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 424/199.1, 232.1;
435/69.1, 69.3, 235.1, 320.1 [IMAGE AVAILABLE]

US PAT NO: 5,766,599 [IMAGE AVAILABLE] L10: 8 of 23

ABSTRACT:
What is described is a modified vector, such as a recombinant poxvirus,
particularly recombinant vaccinia virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open
reading frame encoding a virulence factor. In another embodiment, the
genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential
virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant virus
vaccines.

9. 5,762,938, Jun. 9, 1998, Modified recombinant vaccinia virus and expression vectors thereof; Enzo Paoletti, et al., 424/199.1, 204.1, 205.1, 232.1; 435/320.1; 536/23.72 [IMAGE AVAILABLE]

US PAT NO: 5,762,938 [IMAGE AVAILABLE] L10: 9 of 23

ABSTRACT:
What is described is a modified vector, such as a recombinant poxvirus,
particularly recombinant vaccinia virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open
reading frame encoding a virulence factor. In another embodiment, the
genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential
virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant virus
vaccines.

10. 5,762,921, Jun. 9, 1998, Composition and methods for the treatment
of tumors; Gordon A. Vehar, 424/85.1, 85.2, 85.5, 158.1, 198.1; 514/12;
530/350, 351, 381 [IMAGE AVAILABLE]

US PAT NO: 5,762,921 [IMAGE AVAILABLE] L10: 10 o 23

ABSTRACT:
The invention concerns a method for inducing a selective collapse of the
vasculature of a solid tumor by administering to a patient a therapeutically effective dose of a combination of a compound preventing
the formation of a functional thrombin-thrombomodulin complex and a
cytokine selected from the group of TNF-.beta. (LT), TNF-.alpha., IL-1,
and IFN-.gamma.. The invention further concerns the composition used in
this method.

11. 5,756,103, May 26, 1998, Alvac canarypox virus recombinants comprising heterlogous inserts; Enzo Paoletti, et al., 424/199.1, 204.1, 206.1, 207.1, 208.1, 214.1, 232.1; 435/69.3, 173.3, 235.1, 252.3, 320.
530/350, 826 [IMAGE AVAILABLE]

US PAT NO: 5,756,103 [IMAGE AVAILABLE] L10: 11 o 23

ABSTRACT:
What is described is a modified vector, such as a recombinant poxvirus,
particularly recombinant vaccinia virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open
reading frame encoding a virulence factor. In another embodiment, the
genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential
virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant virus
vaccines.

12. 5,719,127, Feb. 17, 1998, Modified **complement** system regulators;
John P. Atkinson, et al., 514/12; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,719,127 [IMAGE AVAILABLE] L10: 12 o 23

ABSTRACT:
Analogs of regulators of **complement** activation (RCA) proteins which
have altered specificities and affinities for the targets C3b and/or C4b are described. These analogs are obtained by substituting amino acids which effect the binding of these proteins, identified as amino acids 35,
64-65, 92-94 (C4b) and the sequence S-T-K-P-(P-I-C)-Q (C3b) in the CR1
protein can be transferred to corresponding regions of CR1 or of

additional members of the RCA family. Analogs can also be designed by
substituting amino acids which affect the binding of these proteins into
homologous regions of noncorresponding **SCRs** of CR1 or other family
members.

13. 5,679,546, Oct. 21, 1997, Chimeric proteins which block **complement** activation; Jone-Long Ko, et al., 435/69.2, 69.7, 252.3,
320.1; 530/350, 412; 536/23.4 [IMAGE AVAILABLE]

US PAT NO: 5,679,546 [IMAGE AVAILABLE] L10: 13 of 23

ABSTRACT:
The present invention relates to novel chimeric proteins comprising a first polypeptide which inhibits **complement** activation, linked to a
second polypeptide which inhibits **complement** activation, nucleic
acids encoding novel chimeric proteins and methods of reducing inflammation with the administration of the chimeric proteins of the invention.

14. 5,545,619, Aug. 13, 1996, Modified **complement** system regulators;
John P. Atkinson, et al., 514/12; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,545,619 [IMAGE AVAILABLE] L10: 14 of 23

ABSTRACT:
Analogs of regulators of **complement** activation (RCA) proteins which
have altered specificities and affinities for the targets C3b and/or C4b are described. These analogs are obtained by substituting amino acids which effect the binding of these proteins, identified as amino acids 35,
64-65, 92-94 (C4b) and the sequence S-T-K-P-(P-I-C)-Q (SEQ ID NO:1) (C3b)
in the CR1 protein can be transferred to corresponding regions of CR1 or
of additional members of the RCA family. Analogs can also be designed by
substituting amino acids which affect the binding of these proteins into
homologous regions of noncorresponding **SCRs** of CR1 or other family
members.

15. 5,494,807, Feb. 27, 1996, NYVAC vaccinia virus recombinants comprising heterologous inserts; Enzo Paoletti, et al., 435/69.3; 424/199.1, 204.1, 205.1, 218.1, 224.1, 227.1, 229.1, 230.1, 231.1, 232.1, 239.1; 435/235.1, 320.1; 514/2; 530/350, 826 [IMAGE AVAILABLE]

US PAT NO: 5,494,807 [IMAGE AVAILABLE] L10: 15 of 23

ABSTRACT:
What is described is a modified vector, such as a recombinant poxvirus,
particularly recombinant vaccinia virus, having enhanced safety. The modified recombinant virus has nonessential virus-encoded genetic functions inactivated therein so that virus has attenuated virulence. In one embodiment, the genetic functions are inactivated by deleting an open
reading frame encoding a virulence factor. In another embodiment, the
genetic functions are inactivated by insertional inactivation of an open reading frame encoding a virulence factor. What is also described is a vaccine containing the modified recombinant virus having nonessential
virus-encoded genetic functions inactivated therein so that the vaccine has an increased level of safety compared to known recombinant virus
vaccines.

16. 5,472,939, Dec. 5, 1995, Method of treating **complement** mediated
disorders; Douglas T. Fearon, et al., 514/8, 2, 12, 885, 886 [IMAGE AVAILABLE]

US PAT NO: 5,472,939 [IMAGE AVAILABLE] L10: 16 of 23

ABSTRACT:
The present invention relates to the C3b/C4b receptor (CR1) gene and its
encoded protein. The invention also relates to CR1 nucleic acid sequences
and fragments thereof comprising 70 nucleotides and their encoded peptides or proteins comprising 24 amino acids. The invention further provides for the expression of the CR1 protein and fragments thereof. The
genes and proteins of the invention have uses in diagnosis and therapy of
disorders involving **complement** activity, and various immune system or
inflammatory disorders. In specific embodiments of the present invention
detailed in the examples sections infra, the cloning, nucleotide sequence, and deduced amino acid sequence of a full-length CR1 cDNA and
fragments thereof are described. The expression of the CR1 protein and
fragments thereof is also described. Also described is the expression of
a secreted CR1 molecule lacking a transmembrane region. The secreted CR1
molecule is shown to be useful in reducing damage caused by inflammation
and in reducing myocardial infarct size and preventing reperfusion injury.

17. 5,405,946, Apr. 11, 1995, Recombinant protein S variants deficient
in **C4BP** binding activity, compositions and therapeutic methods; John
H. Griffin, et al., 530/380; 435/69.6; 530/830 [IMAGE AVAILABLE]

US PAT NO: 5,405,946 [IMAGE AVAILABLE] L10: 17 of 23

ABSTRACT:
The present invention describes a variant protein **S** **protein** that
is substantially homologous in amino acid residue sequence to wild-type
mature human protein S, which has in vitro anticoagulant activity and has
a reduced ability to bind C4b binding protein (**C4BP**), compositions
containing the variant protein S, and recombinant DNA vectors for expressing the variant protein. Also disclosed are therapeutic methods of
using variant protein S for inhibiting thrombosis, inflammation and the
like conditions ameliorated by protein S.

18. 5,378,464, Jan. 3, 1995, Modulation of inflammatory responses by
administration of GMP-140 or antibody to GMP-140; Rodger P. McEver,
424/143.1; 514/8 [IMAGE AVAILABLE]

US PAT NO: 5,378,464 [IMAGE AVAILABLE] L10: 18 of 23

ABSTRACT:
A method using compounds inhibiting binding reactions involving GMP-140
to modulate an inflammatory response. The method is based on the discovery that GMP-140, released from the storage granules of platelets,
endothelial cells, and megakaryocytes, and redistributed to the surface of the cells within seconds of activation by mediators such as thrombin,
ionophores or histamine, binds to a ligand on neutrophils, and the plasma
proteins C3b and protein S. Adhesion of the cells following activation is
blocked directly by administration of antibody to GMP-140 or its ligand,
or by competitive inhibition by administration of soluble GMP-140, the
GMP-140 ligand, or the specific carbohydrate portion of the ligand bound
by GMP-140.

19. 5,321,123, Jun. 14, 1994, Protein S polypeptides and anti-peptide antibodies that inhibit protein S binding to C4B binding protein, diagnostic systems and therapeutic methods; John H. Griffin, et al., 530/300; 435/7.93; 436/501; 530/324, 325, 327, 328, 329, 830 [IMAGE AVAILABLE]

US PAT NO: 5,321,123 [IMAGE AVAILABLE] L10: 19 of 23

ABSTRACT:
The invention describes protein S polypeptides and anti-PS antibodies capable of inhibiting the binding of proteins to **C4BP**. The peptides
and antibodies are useful in diagnostic methods and systems for purifying
or detecting free protein S. In addition, the polypeptides are useful in therapeutic methods as an anti-coagulant.

20. 5,256,642, Oct. 26, 1993, Compositions of soluble **complement**
receptor 1 (CR1) and a thrombolytic agent, and the methods of use thereof; Douglas T. Fearon, et al., 514/8; 424/94.63, 94.64; 435/215, 216; 514/2; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,256,642 [IMAGE AVAILABLE] L10: 20 of 23

ABSTRACT:
The present invention relates to compositions comprising soluble **complement** receptor 1 (CR1) and a thrombolytic agent. In a specific
embodiment, the thrombolytic agent is anisoylated human plasminogen-streptokinase activator complex (ASPAC). The invention
further relates to methods for treating thrombotic conditions in humans
and animals by administering a composition comprising soluble CR1 and a
thrombolytic agent. In particular, the compositions and methods are useful both for reducing reperfusion injury and ameliorating the other effects of myocardial infarction.

21. 5,252,216, Oct. 12, 1993, Protein purification; Gail Folena-Wasserman, et al., 210/635, 656; 530/380, 413, 416, 417, 420 [IMAGE AVAILABLE]

US PAT NO: 5,252,216 [IMAGE AVAILABLE] L10: 21 o 23

ABSTRACT:
This invention relates to the application of combination chromatography
to the purification of **complement** receptor proteins.

22. 5,221,616, Jun. 22, 1993, Prevention of spontaneous **complement**
activation in mammalian biological fluids; William P. Kolb, et al., 435/18; 436/69 [IMAGE AVAILABLE]

US PAT NO: 5,221,616 [IMAGE AVAILABLE] L10: 22 o 23

ABSTRACT:
Selected polyhydroxyl compounds, comprising monosaccharides, disaccharides and oligosaccharides, as well as certain of their derivatives, are effective in preventing the spontaneous activation of **complement** in vitro. The effect is enhanced in the presence of an
anticoagulant together with a divalent cation chelator. Addition of these
compounds makes it possible to store clinical samples at conventional temperatures from -20.degree. to +22.degree. C. for extended periods prior to performing **complement** protein assays. Effective compounds
are selected through a screening protocol which comprises the use of immunoassays for **complement** fragments together with an algorithm for
computing effectiveness. Polyhydroxyl compounds extend similar protection
from activation to **coagulation** proteins.

23. 5,212,071, May 18, 1993, Nucleic acids encoding a human C3b/C4b
receptor (CR1); Douglas T. Fearon, et al., 435/69.1, 252.3, 320.1; 530/350 [IMAGE AVAILABLE]

US PAT NO: 5,212,071 [IMAGE AVAILABLE] L10: 23 o 23

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            E KLATZMAN, DAVID/IN
L1          2 S E4
            E COEN, JACQUES/IN
            E COHEN, JACQUES/IN
L2          9 S E3
L3         44 S C4BP
L4         44 S C4BP?
L5         22 S L4 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1
L6          0 S L5 AND SCFV?
L7         14 S L5 AND ERYTHROCYTE?
L8         14 S L7 AND (ALPHA OR BETA)
L9         43 S L3 AND (COAGULATION OR COMPLEMENT)
L10        23 S L9 AND (S PROTEIN OR SCR OR SCRS)
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=> s l2 and (coagulation or complement)

L3 103 L2 AND (COAGULATION OR COMPLEMENT)

=> s l3 and erythrocyte?

L4 18 L3 AND ERYTHROCYTE?

=> s l3 and c terminal

L5 1 L3 AND C TERMINAL

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L7 6 L1 AND (ANTI-RH OR ANTI RH)

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L4 18 S L3 AND ERYTHROCYTE?
L5 1 S L3 AND C TERMINAL
L6 0 S L2 AND RATIO
L7 6 S L1 AND (ANTI-RH OR ANTI RH)
L8 4 S L3 AND S PROTEIN?

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PROCESSING COMPLETED FOR L2
L9 46 DUP REM L2 (60 DUPLICATES REMOVED)

=> dup rem l4

PROCESSING COMPLETED FOR L4
L10 8 DUP REM L4 (10 DUPLICATES REMOVED)

=> dup rem l7

PROCESSING COMPLETED FOR L7
L11 2 DUP REM L7 (4 DUPLICATES REMOVED)

=> dup rem l8

PROCESSING COMPLETED FOR L8
L12 4 DUP REM L8 (0 DUPLICATES REMOVED)

=> d l9 ibib abs 1-46

L9 ANSWER 1 OF 46 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1999:144622 BIOSIS
DOCUMENT NUMBER. PREV199900144622
TITLE: Antibody recognition of complement regulatory proteins, factor H, ***CR1*** and ***C4BP*** in antiphospholipid syndrome patients.
AUTHOR(S): Guerin, J. (1); Sim, R. B.; Feighery, C. (1); Jackson, J. (1)
CORPORATE SOURCE: (1) Dep. Immunol., St. James's Hosp., Dublin Ireland
SOURCE: Lupus, (1998) Vol. 7, No. SUPPL. 2, pp. S180. Meeting Info.: 8th International Symposium on Antiphospholipid Antibodies Sapporo, Japan October 6-9, 1998
ISSN: 0961-2033.
DOCUMENT TYPE: Conference
LANGUAGE: English

L9 ANSWER 2 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:267203 CAPLUS
DOCUMENT NUMBER: 126:250213
TITLE: Recombinant heteromultimeric C4 binding protein fusion proteins and their use for vaccines, immunotherapy and diagnosis
INVENTOR(S): Klatzmann, David; Cohen, Jacques
PATENT ASSIGNEE(S): Universite de Reims Champagne Ardennes, Fr.; Universite Pierre et Marie Curie Paris VI
SOURCE: Fr. Demande, 36 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 2736916 | A1 | 19970124 | FR 95-8901 | 19950721 |
| FR 2736916 | B1 | 19970919 | | |
| WO 9704109 | A1 | 19970206 | WO 96-FR1132 | 19960718 |

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

| | | | | |
|---|---|---|---|---|
| CA 2227030 | AA | 19970206 | CA 96-2227030 | 19960718 |
| EP 842282 | A1 | 19980520 | EP 96-926424 | 19960718 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: FR 95-8901 19950721
WO 96-FR1132 19960718
AB Disclosed are recombinant multimeric proteins comprising at least (a) fusion protein A contg. C4 binding protein ( ***C4BP*** ) .alpha. chain C-terminal residues 124-549 and a heterologous protein and (b) fusion protein B contg. ***C4BP*** .beta. chain C-terminal residues 120-235 and a heterologous protein, the proteins A and B binding to each other through the C-terminal domains to form the multimeric protein. Recombinant cells producing the multimeric proteins as well as use of the heteromultimers or cells for fetal-maternal alloimmunization, for therapy or prophylaxis of infections, for therapy of autoimmune diseases, for immunotherapy and for diagnosis are also disclosed. Thus, anti-Rh(D) scFv- ***C4BP*** and CD43 fragment- ***C4BP*** fusion proteins were produced with CHO cells. The heteromultimeric protein formed agglutinated Rh+ erythrocytes.

L9 ANSWER 3 OF 46 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1997:369854 BIOSIS
DOCUMENT NUMBER: PREV199799669057
TITLE: The use of RCA YACs to generate transgenic animals expressing genes of the human regulators of complement activation.
AUTHOR(S): Weiss, E. H.; Sprinks, M. T.; Besenfelder, U.; Cannich, A.; Mueller, S.; Brem, G.
CORPORATE SOURCE: Inst. Anthropol. Humangenet., Ludwig-Maximilians-Univ. Muenchen, Muenchen Germany
SOURCE: Experimental and Clinical Immunogenetics, (1997) Vol. 14, No. 1, pp. 107. Meeting Info.: 6th European Meeting on Complement in Human Disease Innsbruck, Austria March 12-15, 1997
ISSN: 0254-9670.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L9 ANSWER 4 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:479450 CAPLUS
DOCUMENT NUMBER: 125:107075
TITLE: Transgene construct using locus control region upstream of gene of interest, improved expression in transgenic animal, and xenograft implant hyperacute rejection
INVENTOR(S): Colman, Alan
PATENT ASSIGNEE(S): Ppl Therapeutics (Scotland) Ltd., UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9617946 | A1 | 19960613 | WO 95-GB2839 | 1995120 |

W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| AU 9539906 | A1 | 19960626 | AU 95-39906 | 19951206 |

PRIORITY APPLN. INFO.: GB 94-24550 19941206
WO 95-GB2839 19951206
AB The application identifies a problem in the expression of transgenes in transgenic animals which renders the use of transgenic material unsuitable for successful xenograft transplantation. The difficulty identified is the variated expression of the transgene which renders the xenograft vulnerable to hyperacute rejection after implantation. The soln. described is to include a region corresponding to a substantial portion of the region naturally upstream of the gene of interest. Preferably the region includes the locus control region (LCR) for the gene of interest, preferably together with the intervening section which naturally links the LCR to the gene of interest. The transgene construct described is therefore extremely large and is desirably manipulated and amplified using YAC technol.

L9 ANSWER 5 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:607743 CAPLUS
DOCUMENT NUMBER: 125:245269
TITLE: Identification of three physically and functionally distinct binding sites for C3b in human complement factor H by deletion mutagenesis
AUTHOR(S): Sharma, Ajay K.; Pangburn, Michael K.
CORPORATE SOURCE: Department Biochemistry, University Texas Health Science Center, Tyler, TX, 75710-2003, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1996), 93(20), 10996-11001
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human complement factor H controls spontaneous activation of complement in plasma and appears to play a role in distinguishing host cells from activators of the alternative pathway of complement. In both mice and humans, the protein is composed of 20 homologous short consensus repeat (SCR) domains. The size of the protein suggests that portions of the structure outside the known C3b binding site (SCR 1-4) possess a significant biol. role. We have expressed the full-length cDNA of factor H in the baculovirus system and have shown that recombinant protein to be fully active. Mutants of this full-length protein have now been prepd., purified, and examd. for cofactor activity and binding to C3b and heparin. The results demonstrate (i) that factor H has at least three sites that bind C3b, (ii) that one of these sites is located in SCR domains 1-4, as has been shown by others, (iii) that a second site exists in the domain 6-10 region, (i.v.) that a third site resides in the SCR 16-20 region, and (v) that two heparin binding sites exist in factor H, one near SCR 13 and another in the SCR 6-10 region. Functional assays demonstrated that only the first C3b site located in SCR 1-4 expresses factor I cofactor activity. Mutant proteins lacking any one of the three C3b binding sites exhibited 6- to 8-fold redns. in affinity for C3b on sheep erythrocytes, indicating that all three sites contribute to the control of complement activation on erythrocytes. The identification of multiple functionally distinct sites on factor H clarifies many of the heretofore unexplainable behaviors of this protein, including the heterogeneous binding of factor H to surface-bound C3b, the effects of trypsin cleavage, and the

differential control of complement activation on activators and nonactivators of the alternative pathway of complement.

L9 ANSWER 6 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:252939 CAPLUS
DOCUMENT NUMBER: 124:286566
TITLE: Human skeletal myoblasts spontaneously activate allogeneic complement but are resistant to killing
AUTHOR(S): Gasque, Philippe; Morgan, B. Paul; Legoedec, Jocelyne; Chan, Philippe; Fontaine, Marc
CORPORATE SOURCE: Dep. Med. Biochem., Univ. Wales Coll. Med., Cardiff, UK
SOURCE: J. Immunol. (1996), 156(9), 3402-11
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The complement (C) system has previously been implicated in several diseases of muscle. We here report that human myoblasts or rhabdomyosarcoma cell lines spontaneously activate C through the classical pathway, causing release of anaphylatoxins and coating of myoblasts with opsonic C fragments but without causing cell killing. Survival of myoblasts is a consequence of the abundant expression of the membrane C regulatory mols. MCP and CD59, and neutralization of CD59 renders cells susceptible to C killing. The decay-accelerating factor was expressed at a very low level. Myoblasts and rhabdomyosarcoma lines also abundantly express the fluid-phase regulators C1-inhibitor, factor H, C4 binding protein, S-protein, and clusterin and secrete a sol. form of CD59. Expression of membrane and fluid-phase regulators is enhanced by either IFN-.gamma. or TNF-.alpha.. Although myoblasts resist C killing, spontaneous activation of C on these cells may have important consequences in inflammatory diseases of muscle where the generation of anaphylactic and opsonic fragments with recruit and activate inflammatory cells. C activation on myoblasts may also have consequences for the use of these cells as vehicles for gene delivery. Inhibition of C using sol. complement receptor 1 (sCR1) efficiently protected myoblasts from C attack in vitro, and this agent, already being tested in therapy of several C-mediated diseases, might be of value in inflammatory muscle disease and in improving the efficiency of gene delivery.

L9 ANSWER 7 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:708713 CAPLUS
DOCUMENT NUMBER: 126:6135
TITLE: Complement regulatory protein expression by a human oligodendrocyte cell line: cytokine regulation and comparison with astrocytes
AUTHOR(S): Gasque, P.; Morgan, B. P.
CORPORATE SOURCE: Dep. of Medical Biochemistry, Tenovus Building, Cardiff, CF4 4XX, UK
SOURCE: Immunology (1996), 89(3), 338-347
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rat oligodendrocytes spontaneously active complement (C) and lack the C inhibitor CD59. As a consequence, rat oligodendrocytes are susceptible to lysis by autologous C in vitro. Expression of C inhibitors on human oligodendrocytes in vitro and other human glia has yet to be well characterized. We have previously shown expression at the mRNA level of the membrane inhibitors CD59, decay-accelerating factor (DAF; CD55) and membrane cofactor protein (MCP; CD46) in human astrocytes. We here examine the expression of membrane and secreted C inhibitors by the oligodendrocyte cell line, HOG. HOG cells abundantly expressed CD59, assessed at protein and mRNA level, and expressed CAF and MCP, albeit at a lower level. Expression of all three inhibitors was enhanced by incubation with interferon-.gamma. or with phorbol ester (PMA). Complement receptor type 1 ( ***CR1*** ; ***CD35*** ) was neither expressed constitutively nor induced by cytokines. HOG also constitutively secreted C1-inhibitor, S-protein and clusterin. Factor H was secreted only after stimulation with cytokines. C4b binding proteins was expressed at a very low level and was detected only at the mRNA level by reversed transcriptase-polymerase chain reaction (Rt-PCR). For comparison, astrocyte expression of CD59, DAF, MCP and ***CR1*** was confirmed at the mRNA and protein levels. HOG did not activate C spontaneously, as judged by the lack of deposition of C fragments, and were not lysed by C even after inhibition of CD59 and DAF using specific monoclonal antibodies.

L9 ANSWER 8 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:538616 CAPLUS
DOCUMENT NUMBER: 122:263536
TITLE: Chimeric proteins which block complement activation
INVENTOR(S): Ko, Jone Long; Higgins, Paul J.; Yeh, C. Grace
PATENT ASSIGNEE(S): Cytomed, Inc., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9508570 | A1 | 19950330 | WO 94-US10786 | 19940923 |
| W: AU, CA, CN, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 5679546 | A | 19971021 | US 94-310416 | 19940922 |
| AU 9480719 | A1 | 19950410 | AU 94-80719 | 19940923 |
| AU 697167 | B2 | 19981001 | | |
| EP 723555 | A1 | 19960731 | EP 94-931763 | 19940923 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 09502985 | T2 | 19970325 | JP 94-509957 | 19940923 |

PRIORITY APPLN. INFO.: US 93-126596 19930924
US 94-310416 19940922
WO 94-US10786 19940923
AB The present invention relates to novel chimeric proteins comprising a first and a second polypeptides which inhibit complement activation, linked to a second polypeptide which inhibits complement activation selecting from membrane cofactor protein (MCP), decay accelerating factor (DAF), complement receptor 1, factor H, C4b binding protein, or fragments. Nucleic acids encoding the novel chimeric proteins and methods for purifying the chimeric proteins and reducing inflammation with the administration of the chimeric proteins of the invention. In example, a recombinant gene encoding a complement receptor fusion proteins, e.g. MCP-MCP, MCP-DAF and DAF-MCP were mol. cloned and expressed, and a complement activation blocker, CAB-2, was purified and identified by ELISA. The protein cofactor and decay accelerating factor activities were confirmed and inhibition of complement-mediated lysis was tested.

L9 ANSWER 9 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:643347 CAPLUS
DOCUMENT NUMBER: 123:54150
TITLE: Modified truncated complement system regulators for autoimmune disease treatment, transplant rejection suppression, or tissue damage diagnosis
INVENTOR(S): Atkinson, John P.; Hourcade, Dennis; Krych, Malgorzata
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9508343 | A1 | 19950330 | WO 94-US10820 | 19940923 |
| W: AU, CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2171953 | AA | 19950330 | CA 94-2171953 | 19940923 |
| AU 9478424 | A1 | 19950410 | AU 94-78424 | 19940923 |
| AU 691525 | B2 | 19980521 | | |
| EP 730469 | A1 | 19960911 | EP 94-929330 | 19940923 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC NL, PT, SE | | | | |
| JP 09506764 | T2 | 19970708 | JP 94-509968 | 19940923 |

PRIORITY APPLN. INFO.: US 93-126505 19930924
WO 94-US10820 19940923
AB Analogs of regulators of complement activation (RCA) proteins which have altered specificities and affinities for the targets C3b and/or C4b are described. These analogs are obtained by substituting amino acids which affect the complement inhibitory activities of these proteins, substituting, rearranging or adding short consensus repeats (SCRs) or SCR regions to the proteins, deleting amino acid sequences, and combinations thereof.

L9 ANSWER 10 OF 46 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95181440 EMBASE
DOCUMENT NUMBER: 1995181440
TITLE: Evaluation of the relationship between protein S and C4b-binding protein isoforms in hereditary protein S deficiency demonstrating type I and type III deficiencies to be phenotypic variants of the same genetic disease.
AUTHOR: Zoller B.; Garcia de Frutos P.; Dahlback B.
CORPORATE SOURCE: Department of Clinical Chemistry, Malmo General Hospital,S-20502 Malmo, Sweden
SOURCE: Blood, (1995) 85/12 (3524-3531).
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 022 Human Genetics
025 Hematology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Type III protein S deficiency is characterized by a low plasma level of free protein S, whereas the total concentration of protein S is normal. In contrast, both free and total protein S levels are low in type I deficiency. To elucidate the molecular mechanism behind the selective deficiency of free protein S in type III deficiency, the relationship between the plasma concentrations of .beta.-chain containing isoforms of C4b-binding protein ( ***C4BP*** .beta.+) and different forms of protein S (free, bound, and total) was evaluated in 327 members of 18 protein S-deficient families. In normal relatives (n = 190), protein S correlated well with ***C4BP*** .beta.+ with free protein S (96 .+-. 23 nmol/L) being equal to the molar excess of protein S (355 .+-. 65 nmol/L) over ***C4BP*** .beta.+ (275 .+-. 47 nmol/L). In protein S-deficient family members (n = 117), the equimolar relationship between protein S (215 .+-. 50 nmol/L) and ***C4BP*** .beta.+ (228 .+-. 51 nmol/L), together with the high affinity of the interaction, resulted in low levels of free protein S (16 .+-. 10 nmol/L). Free protein S levels were distinctly low in proteinS-deficient members, whereas in 47 of the protein S-deficient individuals, the concentration of total protein S was within the normal range, which fulfills the criteria for type III deficiency. The remaining 70 had low levels of both total and free protein S and, accordingly, would be type I deficient. Coexistence of type I and type III deficiency was found in 14 families, suggesting the two types of protein S deficiency to be phenotypic variants of the same genetic disease. Interestingly, not only protein S but also ***C4BP*** .beta.+ levels were decreased in orally anticoagulated controls and even more so in anticoagulated protein S- deficient members, suggesting that the concentration of ***C4BP*** .beta.+ is influenced by that of protein S. In conclusion, our results indicate that type I and type III deficiencies are phenotypic variants of the same genetic disease and that the low plasma concentrations of free protein S in both types are the result of an equimolar relationship between protein S and ***C4BP*** .beta.+.

L9 ANSWER 11 OF 46 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 95226458 MEDLINE
DOCUMENT NUMBER: 95226458

TITLE: cDNA structure of rabbit C4b-binding protein alpha-chain.
Preserved sequence motive in complement regulatory protein
modules which bind C4b.
AUTHOR: Garcia de Frutos P; Dahlback B
CORPORATE SOURCE: Department of Clinical Chemistry, University of Lund, Malmo
General Hospital, Sweden..
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA, (1995 Apr 4) 1261 (2) 285-9.
Journal code: A0W. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-Z35490
ENTRY MONTH: 199507
AB A full length cDNA clone for the alpha-chain of the rabbit complement
regulatory protein C4b-binding protein ( ***C4BP*** ) was isolated from
a liver cDNA library. The clone encoded an open reading frame of 597 amino
acids, which included a signal peptide, eight short consensus repeats
(SCR) and a carboxy terminal non-repeat region. Gel filtration of rabbit
plasma and testing of fractions for factor I cofactor activity ( ***C4BP*** -like) revealed two peaks of activity, the one with highest
molecular weight corresponding in size to that of human C4b-binding
protein. Comparison of the rabbit ***C4BP*** alpha-chain sequence with
other SCR containing C3b/C4b binding proteins revealed highest sequence
similarities between the second SCRs in ***C4BP*** from rabbit, human
and murine species and SCRs at corresponding position in complement
receptor 1 ( ***CR1*** ) whereas in decay accelerating factor (DAF), the
third SCR was most similar. A conserved sequence motive was identified in
these C4b-binding SCRs.

L9 ANSWER 12 OF 46 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 95:258922 SCISEARCH
THE GENUINE ARTICLE: QQ952
TITLE: CDNA STRUCTURE OF RABBIT C4B-BINDING PROTEIN ALPHA-CHAIN -
PRESERVED SEQUENCE MOTIVE IN COMPLEMENT REGULATORY PROTEIN
MODULES WHICH BIND C4B
AUTHOR: DEFRUTOS P G; DAHLBACK B (Reprint)
CORPORATE SOURCE: LUND UNIV, MALMO GEN HOSP, DEPT CLIN CHEM, S-21401 MALMO,
SWEDEN (Reprint); LUND UNIV, MALMO GEN HOSP, DEPT CLIN
CHEM, S-21401 MALMO, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: BIOCHIMICA ET BIOPHYSICA ACTA-GENE STRUCTURE AND
EXPRESSION, (04 APR 1995) Vol. 1261, No. 2, pp. 285-289.
ISSN: 0167-4781.
DOCUMENT TYPE: Note; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 26
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB A full length cDNA clone for the alpha-chain of the rabbit complement
regulatory protein C4b-binding protein ( ***C4BP*** ) was isolated from
a liver cDNA library. The clone encoded an open reading frame of 597 amino
acids, which included a signal peptide, eight short consensus repeats
(SCR) and a carboxy terminal non-repeat region. Gel filtration of rabbit
plasma and testing of fractions for factor I cofactor activity ( ***C4BP*** -like) revealed two peaks of activity, the one with highest
molecular weight corresponding in size to that of human C4b-binding
protein. Comparison of the rabbit ***C4BP*** alpha-chain sequence with
other SCR containing C3b/C4b binding proteins revealed highest sequence
similarities between the second SCRs in ***C4BP*** from rabbit, human
and murine species and SCRs at corresponding position in complement
receptor 1 ( ***CR1*** ) whereas in decay accelerating factor (DAF), the
third SCR was most similar. A conserved sequence motive was identified in
these C4b-binding SCRs.

L9 ANSWER 13 OF 46 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1995:381172 BIOSIS
DOCUMENT NUMBER: PREV199598395472
TITLE: A soluble multimeric C3b/C4b receptor ( ***CR1*** , ***CD35*** ) using a general purpose C4 terminal ***C4BP*** multimerising systems.
AUTHOR(S): Oudin, S. (1); Tonye-Libyh, M. (1); Goossens, D.; Gupta, N. (1); Cornillet, P. (1); Tabary, T. (1); Philbert, F. (1); Bacchi, V.; Fischer, E.; Rouger, P.; Kazatchkine, M. D.; Klatzmann, D.; Cohen, J. H. M. (1)
CORPORATE SOURCE: (1) Lab. Immunol., Pole Biomolecules, Reimes, Paris France
SOURCE: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY.. (1995) pp. 95.
The 9th International Congress of Immunology.
Publisher: 9th International Congress of Immunology San Francisco, California, USA.
Meeting Info.: Meeting Sponsored by the American Association of Immunologists and the International Union of
Immunological Societies San Francisco, California, USA July
23-29, 1995
DOCUMENT TYPE: Conference
LANGUAGE: English

L9 ANSWER 14 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1995:130566 CAPLUS
DOCUMENT NUMBER: 122:4393
TITLE: Complement regulatory proteins of herpesvirus saimiri
and their similarity to other complement-regulating proteins
INVENTOR(S): Fleckenstein, Bernhard; Albrecht, Jens-Christian
PATENT ASSIGNEE(S): Alexion Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9416062 | A1 | 19940721 | WO 93-US672 | 19930112 |

W: CA, US
AB Gene sequences for three complement regulatory proteins encoded within the
genome of Herpesvirus Saimiri (HVS) are disclosed, namely, mCCPH, sCCPH,
and HVS-15. MCCPH and sCCPH share substantial homol. with the human
complement inhibitory proteins factor H, ***CD35*** , CD46, CD55, and
***C4bp*** which inhibit C3 convertase activity in the complement
cascade. HVS-15 shares substantial homol. with the human complement
inhibitory protein CD59 which inhibits formation of the membrane attack
complex of the complement system. The gene sequences and corresponding
proteins can be used a therapeutic agents to control the complement arm of
the immune system.

L9 ANSWER 15 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1994:280266 CAPLUS
DOCUMENT NUMBER: 120:280266
TITLE: Delivery of proteins by intermembrane transfer for preaccommodation of xenogeneic organ transplants and
other purposes
INVENTOR(S): Byrne, Guerard W.; Kooyman, David Lee; Logan, John
Steele
PATENT ASSIGNEE(S): DNX Biotherapeutics, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9406903 | A1 | 19940331 | WO 93-US8889 | 19930922 |

W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP,
KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD,
SE, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
EP 662125 A1 19950712 EP 93-922259 19930922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC NL, PT, SE
JP 08501451 T2 19960220 JP 93-508379 19930922
AU 671158 B2 19960815 AU 93-51325 19930922
FI 9501325 A 19950509 FI 95-1325 19950321
NO 9501074 A 19950519 NO 95-1074 19950321
PRIORITY APPLN. INFO.: US 92-948521 19920922
WO 93-US8889 19930922
AB GPI-linked proteins are transferred, esp. in vivo, from vertebrate carrier
cells to cells of a target vertebrate tissue. For example, for purposes
of xenogeneic transplantation, cells bearing complement inhibition
factor(s) specific for the recipient species, e.g., genetically engineered
red blood cells, are incubated with transplantable cells of a second,
discordant donor species until transfer of the factor(s) occurs. The
transfer may occur in vivo or in vitro, and the factor-bearing cells may
be normal cells of the recipient species, or genetically engineered cells
of the donor species which express a gene encoding a complement inhibition
factor(s) of the recipient species, e.g., DAF, CD59, or others. The
method is particularly useful in modifying pig organs (kidney, heart,
etc.) for xenotransplantation into humans.

L9 ANSWER 16 OF 46 MEDLINE
ACCESSION NUMBER: 93315479 MEDLINE
DOCUMENT NUMBER: 93315479
TITLE: The human C4b-binding protein beta-chain gene.
AUTHOR: Hillarp A; Pardo-Manuel F; Ruiz R R; Rodriguez de Cordoba
S; Dahlback B
CORPORATE SOURCE: Department of Clinical Chemistry, University of Lund, Malmo
General Hospital, Sweden..
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Jul 15) 268 (20)
15017-23.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-L11244; GENBANK-L11245; GENBANK-L11246
ENTRY MONTH: 199310
AB Human complement component C4b-binding protein ( ***C4BP*** ) is
composed of seven alpha-chains and one beta-chain. The alpha- and
beta-chains are homologous and both contain multiple copies of short
consensus repeats (SCR) and in addition carboxyl-terminal non-repeat
regions. Each of the alpha-chains contains a binding site for C4b, whereas
the beta-chain binds protein S, a vitamin K-dependent protein involved in
the regulation of blood coagulation. The alpha- and beta-chain genes are
closely linked in the regulators of complement activation gene cluster on
the long arm of human chromosome 1, band 1q32. The human beta-chain gene
which has now been characterized was found to span more than 10 kilobases
of DNA. The presence of at least two different beta-chain gene transcripts
was suggested by the isolation of two new cDNA clones which contained
different sequences in their extended 5'-untranslated regions. Northern
blot analysis demonstrated that the two clones represented distinct
beta-chain mRNAs with different 5' end sequences. One class of beta-chain
mRNA (denoted A19) was found to be encoded by six exons and primer
extension, and S1 nuclease protection assays revealed multiple closely
spaced transcription start sites for this mRNA class. Its 5'-untranslated
region and signal peptide was encoded by the first exon. The second class
of mRNA (denoted A12) had a different transcription start site and its
5'-untranslated region was derived from at least three exons out of which
the last one was formed by utilization of an acceptor splice site within
the first A19 exon. Exons encoding the mature beta-chain and the
3'-untranslated region were common to both classes of mRNA. The beta-chain
contains three SCRs, out of which the first and second are encoded by

individual exons, whereas two exons encode the third SCR. The exon
encoding the carboxyl-terminal part of the third SCR also encodes 14 amino
acids of the non-repeat region. The last exon encodes the remaining 46
carboxyl-terminal amino acids and the entire 3'-untranslated region. The
elucidation of the organization of the beta-chain gene provides insight
into the sophisticated molecular structure of ***C4BP*** and a basis
for future structural and functional studies.

L9 ANSWER 17 OF 46 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 92144596 MEDLINE
DOCUMENT NUMBER: 92144596
TITLE: Segment spanning residues 727-768 of the complement C3
sequence contains a neoantigenic site and accommodates the
binding of ***CR1*** , factor H, and factor B.
AUTHOR: Becherer J D; Alsenz J; Esparza I; Hack C E; Lambris J D
CORPORATE SOURCE: Basel Institute for Immunology, Switzerland.
SOURCE: BIOCHEMISTRY, (1992 Feb 18) 31 (6) 1787-94.
Journal code: A0G. ISSN: 0006-2960.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
AB ***CR1*** , CR2, DAF, MCP, factor H, ***C4bp*** , factor B, and C3
are members of a family of structurally related molecules, the majority of
which belong to the complement system. Several of these molecules also
share functional features such as cofactor and decay/dissociation activity
and compete with one another in binding to C3b. Since factor H appears to
bind to multiple sites in C3, we investigated the relationship between the
factor H- and ***CR1*** -binding sites in C3b. Factor H binding to C3b
is inhibited by either the C3c or C3d fragments, and addition of both
fragments together augments this inhibition. One monoclonal anti-C3c
antibody, anti-C3-9, which recognizes a neoantigenic epitope expressed
upon cleavage to C3 to C3b, inhibited both factor H and ***CR1***
binding to EC3b cells. This monoclonal antibody (MoAb) also inhibited
factor B binding to EC3b. Two observations further supported our
hypothesis that these molecules bind to proximal sites in C3b. First, a
synthetic peptide spanning this region of C3b (C3(727-768)) inhibited
factor H binding. Second, antibodies raised against this peptide inhibited
binding to ***CR1*** , factor H, and factor B to C3b. These data show
that H binds to at least two sites in C3b: the site in the C3c fragment is
within the identified ***CR1*** -binding domain while the site in the
C3d fragment surrounds the CR2-binding site.(ABSTRACT TRUNCATED AT 250
WORDS)

L9 ANSWER 18 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:649734 CAPLUS
DOCUMENT NUMBER: 117:249734
TITLE: Complement activation in the follicular light zone of
human lymphoid tissues
AUTHOR(S): Yamakawa, M.; Imai, Y.
CORPORATE SOURCE: Sch. Med., Yamagata Univ., Yamagata, 900-23, Japan
SOURCE: Immunology (1992), 76(3), 378-84
CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A comparative immunohistochem. study of the distribution pattern of
complement components and regulatory proteins within secondary lymphoid
follicles was performed by the immunoperoxidase technique. Fifteen
lymphoid tissues including appendices, Peyer's patches and tonsils were
analyzed. Sixty secondary lymphoid follicles with evident polarity, i.e.,
the distinct coexistence of a light zone, dark zone and mantle zone in the
same lymphoid follicle, were tested with single antibodies. The light
zones were consistently immunostained in a dendritic meshwork pattern with
all antibodies. The immunostaining patterns were classified into two
major groups based on the immunoreactivity of the dark zone. One
immunostaining pattern was characterized by no immunostaining of the dark
zone to the majority of the antigens. The second group was characterized
by a diffusely weak to moderate dendritic meshwork pattern of the dark
zone to some immunostaining for C9 (monoclonal), S-protein, and DF-DRC1,
and all immunostaining of ***CR1*** ( ***CD35*** ), Ber-Mac-DRC (
***CD35*** ), CR2(CD21), and R4/23. All four complement regulatory
proteins were localized by immunoelectron microscopy attached to the cell
surface of the cells, including follicular dendritic cells, in the light
zone. The data indicate that there is an evident functional difference
between the light zone and the dark zone, and that complete activation of
the complement system occurs only in the light zone.

L9 ANSWER 19 OF 46 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 92155718 MEDLINE
DOCUMENT NUMBER: 92155718
TITLE: Analysis of the human regulators of complement activation
(RCA) gene cluster with yeast artificial chromosomes (YACs).
AUTHOR: Hourcade D; Garcia A D; Post T W; Taillon-Miller P; Holers
V M; Wagner L M; Bora N S; Atkinson J P
CORPORATE SOURCE: Howard Hughes Medical Institute Laboratories, Washington
University School of Medicine, St. Louis, Missouri 63110.
SOURCE: GENOMICS, (1992 Feb) 12 (2) 289-300.
Journal code: GEN. ISSN: 0888-7543.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK; GENBANK-M73721; GENBANK-M73722; GENBANK-M73723;
GENBANK-M73448; GENBANK-M73449; GENBANK-M73450;
GENBANK-M73451; GENBANK-M73452; GENBANK-M73453;
GENBANK-M73454
ENTRY MONTH: 199205
AB The human regulators of complement activation gene cluster (RCA cluster)
have been partially characterized with yeast artificial chromosomes
(YACs). While the data confirm many points previously elucidated, the
finer resolution of YAC mapping has allowed the discovery and/or
localization of partial gene duplications, the determination of gene
orientations, and the measurement of gaps between known genes. Here nine
overlapping YACs that encompass a genomic region of 800 kb, encoding four
RCA genes and three gene-like elements, are described. The encoded genes
and two of the gene-like elements share the same orientation and are
ordered (5' to 3') DAF, CR2, ***CR1*** , MCP-like, ***CR1*** -like,
and MCP. A ***C4bp*** -like region lies upstream from DAF and is likely
to correspond to one recently observed by F. Pardo-Manuel, J. Rey-Campos,
A. Hillarp, B. Dahlback, and S. Rodriguez de Cordoba (1990, Proc. Natl.
Acad. Sci. USA 87: 4529-4533). MCP-like, a new genetic element, was
discovered and found to be homologous to the 5' portion of the MCP gene.
Two large gaps of 85 kb (between CR2 and DAF) and 110 kb (between DAF and
the ***C4bp*** -like element) could carry additional RCA genes. The
arrangement of ***CR1*** , MCP-like, ***CR1*** -like, and MCP, in
that order, strongly suggests that this region was generated by a single
duplication of neighboring ***CR1*** / ***CR1*** -like and
MCP/MCP-like forerunners. The RCA YACs will now serve as convenient DNA
sources for the subcloning and further characterization of this region.

L9 ANSWER 20 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:52936 CAPLUS
DOCUMENT NUMBER: 116:52936
TITLE: C4 binding protein fusions with therapeutically useful
proteins
INVENTOR(S): Pasek, Mark P.; Winkler, Gunther; Liu, Theresa R.
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9111461 | A1 | 19910808 | WO 91-US567 | 19910128 |
| W: AU, CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | |
| AU 9173288 | A1 | 19910821 | AU 91-73288 | 19910128 |
| EP 465633 | A1 | 19920115 | EP 91-903951 | 19910128 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE | | | | |
| JP 04506460 | T2 | 19921112 | JP 91-504137 | 19910128 |

PRIORITY APPLN. INFO.: US 90-470888 19900126
WO 91-US567 19910128
AB The complement C4 binding protein ( ***C4bp*** ) is used in fusion
proteins with therapeutic proteins to ensure targetting of the fusion
protein to the blood and to prolong serum half-life. In particular, the
short consensus repeats of the N-terminal region are used. The primary
aim is to provide ***CD4*** antigens for use in the treatment of AIDS.
A cDNA for ***C4bp*** was cloned by polymerase chain reaction
amplification of the mRNA and subloned into the animal expression vector
pJOD-10. When the cloned gene was expressed in COS-7 cells a heptameric
***C4bp*** of the correct conformation but lacking the S protein-binding
subunit was produced. Chimeric genes based upon this cDNA and one
encoding sol. ***CD4*** antigen were constructed and expressed in
COS-7 cells. The purified fusion proteins were shown to form multimers
and to bind the glycoprotein gp120 of HIV in vitro. Conditioned medium
from producer cells prevented syncytia formation by HIV-infected cells.

L9 ANSWER 21 OF 46 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 92017905 MEDLINE
DOCUMENT NUMBER: 92017905
TITLE: Preferential inactivation of the C5 convertase of the alternative complement pathway by factor I and membrane
cofactor protein (MCP).
AUTHOR: Seya T; Okada M; Matsumoto M; Hong K S; Kinoshita T;
Atkinson J P
CORPORATE SOURCE: Department of Immunology, Center for Adult Diseases Osaka,
Japan.
SOURCE: MOLECULAR IMMUNOLOGY, (1991 Oct) 28 (10) 1137-47.
Journal code: NG1. ISSN: 0161-5890.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199201
AB Human C3b bound to the ghost of sheep erythrocytes (E*) via activation of
the alternative complement pathway (E*AC3b) consists of four major
constituents on SDS-PAGE of 350, 260, 210 and 180 kDa. 350 kD C3b is a
dimeric form of C3b in which the alpha' chain of one C3b binds covalently
to that of the other C3b. This complex is presumed to serve as a core for
the alternative pathway C5 convertase. The other C3b populations are
monomers complexed with membrane proteins or sugars. Using E*AC3b (C3b
labeled) as a substrate, we have investigated functional properties of
membrane cofactor protein (MCP), which is an integral membrane protein
with C3b-binding and factor I-dependent cofactor activities. In
conjunction with factor I, MCP was found to degrade the protein-bound C3b
preferentially including the 350 kDa dimer. There was a similar but lesser
tendency of this selective cleavage of C3b-dimer by ***CR1*** but not
by factor H or ***C4bp*** . In contrast to ***CR1*** and factor H,

detergent solubilization of EAC3b was required for MCP to fully express its cofactor activity for this selective degradation of C3b. We next separated the C3b dimer from the monomers and assessed their ability to assemble the alternative C5 convertase. The C3b dimer but not the monomers expressed C5 convertase activity following the addition of factors B and D, C5 and Ni2+. Kinetic analysis of the degradation of the C3b dimer by MCP and factor I suggested that only one C3b was efficiently converted to C3bi and this occurred concomitant with a decrease in C5 convertase activity. These results suggest that MCP has the ability to more efficiently interact with protein-bound C3b and that this may relate as well to its preferential ability to irreversibly inactivate the C5 convertase.

L9 ANSWER 22 OF 46 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 91287723 MEDLINE
DOCUMENT NUMBER: 91287723
TITLE: Regulatory system of guinea-pig complement C3b: tests for compatibility of guinea-pig factors H and I with human factors.
AUTHOR: Seya T; Okada M; Hazeki K; Nagasawa S
CORPORATE SOURCE: Department of Immunology, Center for Adult Diseases, Osaka, Japan..
SOURCE: MOLECULAR IMMUNOLOGY, (1991 Apr-May) 28 (4-5) 375-82.
Journal code: NG1. ISSN: 0161-5890.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199110
AB Two proteins that are involved in cleavage of methylamine-treated C3 of guinea-pig origin (C3(MA)gp) have been isolated from guinea-pig serum. One of them functioned as a cofactor of human factor I (Ihu) for cleavage of C3(MA)gp and its molecular size was 150 kDa. The other was functionally pure and able to cleave C3(MA)gp together with human factor H (Hhu). They appear to be analogous to human factors H and I in the guinea-pig and will be referred to as Hgp and Igp. Methylamine-treated human C3 [C3(MA)hu] was not a compatible substrate for Hgp or Igp: little cleavage of C3(MA)hu was observed if human factor H (Hhu) or I was substituted with the guinea-pig counterpart. C3(MA)gp, on the other hand, served as a substrate, though less efficiently, for Hhu and Ihu. Human C4b-binding protein ( ***C4bp*** ) and membrane cofactor protein (MCP) as well as Hhu could participate in cleavage of C3(MA)gp by Igp or Ihu. In these assays, C3(MA)gp was degraded again less efficiently than C3(MA)hu. Interestingly, human C3b/C4b receptor ( ***CR1*** ) mediated factor I-dependent cleavage of C3(MA)hu and C3(MA)gp to a similar extent regardless the sources of factor I. These results suggest that factor I-dependent C3b regulatory system is species-specific except in the case of ***CR1*** , which may function as a cofactor irrespective of species.

L9 ANSWER 23 OF 46 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 89094254 MEDLINE
DOCUMENT NUMBER: 89094254
TITLE: Structural gene for human membrane cofactor protein (MCP) of complement maps to within 100 kb of the 3' end of the C3b/C4b receptor gene.
AUTHOR: Bora N S; Lublin D M; Kumar B V; Hockett R D; Holers V M; Atkinson J P
CORPORATE SOURCE: Howard Hughes Medical Institute Laboratories, Washington University School of Medicine, St. Louis, Missouri 63110.
CONTRACT NUMBER: RO1-AI19642 (NIAID)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1989 Feb 1) 169 (2) 597-602.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198904
AB The structural gene for membrane cofactor protein (MCP), a widely distributed C3b/C4b binding regulatory glycoprotein of the complement system, has been mapped to the same locus as the structural genes for ***CR1*** , CR2, DAF, and ***C4bp*** . The order of the genes within an approximately 800-kb DNA fragment on the long arm of chromosome 1 is MCP- ***CR1*** -CR2-DAF- ***C4bp*** . Further, the MCP gene maps to within 100 kb of 3' end of the ***CR1*** gene.

L9 ANSWER 24 OF 46 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 89277343 EMBASE
DOCUMENT NUMBER: 1989277343
TITLE: Complexity of MHC class III genes and complement polymorphism.
AUTHOR: Rittner C.; Schneider P.M.
CORPORATE SOURCE: Institut fur Rechtsmedizin, Johannes Gutenberg-Universitat, 6500 Mainz, Germany
SOURCE: Immunology Today, (1989) 10/12 (401-403). ISSN: 0167-4919 CODEN: IMTOD8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In July, a comparatively small group of geneticists from 23 countries met, first in Mainz and again in Berlin at the Immunology Congress, to have a closer look at the major histocompatibility complex (MHC) class III genes and other complement polymorphisms. Class III genes include not only complement but also other loci, like 21-hydroxylase (21-OH) A and B, tumour necrosis factor (TNF) .alpha. and .beta., and duplicated genes of heat shock protein 70 (HSP70), with no obvious functional relationship. On the other hand, complement loci are also found on chromosome 1 (H, ***C4BP*** , ***CR1*** , C8A and B), chromosome 9 (C8G: J. Sodetz, Columbia), and chromosome 19 (C3). Curiously enough, MHC-linked complement genes still attract most attention, probably because evolution, deficiency and disease seem to have a causal relationship. These observations have been the subject of speculations from both the neutralist (J. Klein, Tubingen) and selecionist (T. Meo, Paris) point of view.

L9 ANSWER 25 OF 46 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 88187597 MEDLINE
DOCUMENT NUMBER: 88187597
TITLE: Organization of the genes encoding complement receptors type 1 and 2, decay-accelerating factor, and C4-binding protein in the RCA locus on human chromosome 1.
AUTHOR: Carroll M C; Alicot E M; Katzman P J; Klickstein L B; Smith J A; Fearon D T
CORPORATE SOURCE: Department of Pediatrics, Harvard Medical School, Boston, Massachusetts 02115.
CONTRACT NUMBER: AI-22833 (NIAID)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Apr 1) 167 (4) 1271-80.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198807
AB The organization and physical linkage of four members of a major complement locus, the RCA locus, have been determined using the technique of pulsed field gradient gel electrophoresis in conjunction with Southern blotting. The genes encoding ***CR1*** , CR2, DAF, and ***C4bp*** were aligned in that order within a region of 750 kb. In addition, the 5' to 3' orientation of the ***CR1*** gene (5' proximal to CR2) was determined using 5'- and 3'-specific DNA probes. The proximity of these genes may be related to structural and functional homologies of the protein products. Overall, a restriction map including 1,500 kb of DNA was prepared, and this map will be important for positioning of additional coding sequences within this region on the long arm of chromosome 1.

L9 ANSWER 26 OF 46 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 88171282 MEDLINE
DOCUMENT NUMBER: 88171282
TITLE: Structure of the human B lymphocyte receptor for C3d and the Epstein-Barr virus and relatedness to other members of the family of C3/C4 binding proteins [published erratum appears in J Exp Med 1988 Nov 1;168(5):1953-4].
AUTHOR: Weis J J; Toothaker L E; Smith J A; Weis J H; Fearon D T
CORPORATE SOURCE: Department of Rheumatology and Immunology, Brigham and Women's Hospital, Boston, Massachusetts.
CONTRACT NUMBER: AM-35907 (NIADDK)
AI-23401 (NIAID)
AI-22833 (NIAID)
+
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Mar 1) 167 (3) 1047-66.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-Y00649
ENTRY MONTH: 198807
AB Human complement receptor type 2 (CR2) is the B lymphocyte receptor for C3d and the Epstein-Barr virus. This protein is also a member of a family of C3b/C4b binding proteins that regulate complement activation, comprise tandemly repeated 60-75 amino acid sequences, and whose genes map to band q32 on chromosome 1. Overlapping cDNA clones encoding the entire human CR2 protein have been isolated from a human tonsillar cDNA library. The derived amino acid sequence of 1,032 residues encodes a peptide of 112,716 mol wt. A signal peptide was identified, followed by 15 copies of the short consensus repeat (SCR) structure common to the C3/C4 binding protein family. The entire extracellular portion of the protein comprised SCRs, thus, the ligand binding sites both for C3d and the EBV protein gp350/220 are positioned within this structure. Immediately following the final SCR was a transmembrane sequence of 24 amino acids and a cytoplasmic region of 34 amino acids. One of five cDNA clones isolated contained an additional SCR, providing evidence for alternative mRNA splicing or gene products of different human alleles. The CR2 cDNAs were used to isolate CR2-specific genomic phage. The entire CR2 coding sequences were found within 20 kb of human DNA. Analysis of the CR2 cDNA sequence indicated that CR2 contained internally homologous regions and suggested that CR2 arose by duplication of a primordial gene sequence encoding four SCRs. Comparison of the CR2 peptide sequence with those of other members of the gene family has identified many regions highly homologous with human ***CR1*** , fewer with ***C4bp*** and decay accelerating factor, and very few with factor H, and suggested that CR2 and ***CR1*** arose by duplication of the same ancestral gene sequence. The homology between CR2 and ***CR1*** extended to the transmembrane and cytoplasmic regions, suggesting that these sequences were derived from a common membrane-bound precursor.

L9 ANSWER 27 OF 46 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 89127291 MEDLINE
DOCUMENT NUMBER: 89127291
TITLE: Structural and functional relationships among receptors and regulators of the complement system.
AUTHOR: Dierich M P; Schulz T F; Eigentler A; Huemer H; Schwable W
CORPORATE SOURCE: Institut fur Hygiene, University of Innsbruck, Austria..
SOURCE: MOLECULAR IMMUNOLOGY, (1988 Nov) 25 (11) 1043-51. Ref: 90

Journal code: NG1. ISSN: 0161-5890.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198905
AB The classical and alternative pathway of complement activation are
regulated by a series of fluid phase and cell-bound factors, some of which
at the same time serve as receptors for fragments of C3 and C4. These
molecules are factor H, ***CR1*** (C3b/C4b receptor), CR2 (C3d/EBV
receptor), ***C4BP*** (C4b binding protein), DAF (decay accelerating
factor), MCP (membrane cofactor protein; earlier designated p45/70), CR3
(iC3b receptor or Mac-1) and CR4 (protein 150/95). Due to structural,
genetic and functional features these factors are members of one or
several newly recognized large families of proteins: (1) molecules with 60
amino acids long repeats (H, ***CR1*** , CR2, ***C4BP*** , DAF); (2)
proteins with 1,2-diacylglycerol membrane anchoring (DAF); (3) proteins
with a heterodimer structure and preference for ligands containing the
tripeptide arginine-glycine-asparagine (CR3, CR4). Recognizing the above
mentioned regulators and receptors of the complement system as belonging
to these protein families opens new perspectives for further genetic and
functional research of mutual interest to complement and noncomplement
scientists.

L9 ANSWER 28 OF 46 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 88154754 MEDLINE
DOCUMENT NUMBER: 88154754
TITLE: A physical map of the human regulator of complement
activation gene cluster linking the complement genes
***CR1*** , CR2, DAF, and ***C4BP*** .
AUTHOR: Rey-Campos J; Rubinstein P; Rodriguez de Cordoba S
CORPORATE SOURCE: Department of Immunogenetics, New York Blood Center 10021.
CONTRACT NUMBER: DK-19631-11 (NIDDK)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1988 Feb 1) 167 (2)
664-9.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198806
AB We report the organization of the human genes encoding the complement
components C4-binding protein ( ***C4BP*** ), C3b/C4b receptor (
***CR1*** ), decay accelerating factor (DAF), and C3dg receptor (CR2)
within the regulator of complement activation (RCA) gene cluster. Using
pulsed field gel electrophoresis analysis these genes have been physically
linked and aligned as ***CR1*** -CR2-DAF- ***C4BP*** in an 800-kb
DNA segment. The very tight linkage between the ***CR1*** and the
***C4BP*** loci, contrasted with the relative long DNA distance between
these genes, suggests the existence of mechanisms interfering with
recombination within the RCA gene cluster.

L9 ANSWER 29 OF 46 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 89151487 MEDLINE
DOCUMENT NUMBER: 89151487
TITLE: The molecular genetics of components of the complement
system.
AUTHOR: Campbell R D
SOURCE: BAILLIERES CLINICAL RHEUMATOLOGY, (1988 Dec) 2 (3) 547-75.
Ref: 172
Journal code: CRY. ISSN: 0950-3579.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198906
AB Rapid progress has been made recently on the elucidation of the structural
components of the complement system by the application of recombinant DNA
techniques. The derived amino acid sequences of most of the complement
proteins are now available through cDNA cloning, and significant progress
has been made in the discovery of the genetic organization of the
corresponding genes. The linkage of some of the complement component genes
has been established through the study of phenotypic genetics. Of
particular interest has been the mapping of two clusters of genes which
encode proteins involved in the activation of C3. C2, C4 and factor B,
three of the structural components of the classical and alternative
pathway C3 convertases, are encoded by genes which map to the MHC on human
chromosome 6. The linkage of the genes with each other in a 100 kb segment
of DNA has been established through the isolation of overlapping cosmid
clones of genomic DNA, and PFGE has defined the molecular map position of
these genes within the class III region of the MHC. The regulatory
proteins factor H, ***C4BP*** , ***CR1*** and DAF, which are
involved in the control of C3 convertase activity, are encoded by
closely-linked genes (termed the regulators of complement activation or
RCA linkage group) that have been mapped to human chromosome 1. PFGE has
defined the linkage of the ***CR1*** , ***C4BP*** and DAF genes,
together with the CR2 gene in an 800 kb segment of DNA, and it is clear
that this technique will eventually be applied to the molecular mapping of
other complement genes in relation to their flanking loci. Polymorphism is
a feature of many of the complement proteins, especially those encoded by
genes in the MHC class III region. Of these, C4 is by far the most
polymorphic, and differences in gene size and gene number, in addition to
the functional and antigenic differences in the gene products, have been
recognized. Null alleles at either of the C4 loci are rather common and
may be important susceptibility factors in some HLA-associated diseases,
particularly SLE. The molecular basis of complement deficiency states has
begun to be elucidated. In many cases, the deficiency is not caused by a
major gene deletion or rearrangement, and techniques which detect single
point mutations in DNA (Cotton et al, 1988) will have to be applied to
fully characterize the nature of the defect.

L9 ANSWER 30 OF 46 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88262883 EMBASE
DOCUMENT NUMBER: 1988262883
TITLE: Coagulation factor XIII B subunit is encoded by a gene
linked to the regulator of complement activation (RCA) gene
cluster in man.
AUTHOR: De Cordoba S.R.; Rey-Campos J.; Dykes D.D.; McAlpine P.J.;
Wong P.; Rubinstein P.
CORPORATE SOURCE: Department of Immunogenetics, New York Blood Center, New
York, NY 10021, United States
SOURCE: Immunogenetics, (1988) 28/6 (452-454).
ISSN: 0093-7711 CODEN: IMNGBK
COUNTRY: Germany
DOCUMENT TYPE: Journal; Journal
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We have performed linkage analysis to determine the genetic relationship
between the loci coding for coagulation factor XIII B (F13B) and the
regulator of complement activation (RCA) gene cluster, comprised of the
loci encoding C3b/C4b-receptor ( ***CR1*** ), C3d/Epstein-Barr
virus-receptor (CR2), decay accelerating factor (DAF), C4b-binding protein
( ***C4BP*** ), and factor H (HF), as the products of these six loci
show structural similarities. Here we report that the human F13B gene is
also a member of RCA gene cluster and that it maps in close proximity to
the gene encoding complement factor H.

L9 ANSWER 31 OF 46 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 88256042 MEDLINE
DOCUMENT NUMBER: 88256042
TITLE: Structure and function of a cell-associated complement
regulatory protein, membrane cofactor protein (MCP).
AUTHOR: Seya T
CORPORATE SOURCE: Department of Immunology, Center for Adult Diseases,
Osaka..
SOURCE: HOKKAIDO IGAKU ZASSHI. HOKKAIDO JOURNAL OF MEDICAL SCIENCE,
(1988 Mar) 63 (2) 259-68.
Journal code: GA9. ISSN: 0367-6102.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198810
AB Based on evidence suggesting that human leukocytes have factor I cofactor
activity that is distinct from C3b/C4b receptor ( ***CR1*** ), we
purified the cofactor protein from several human leukocyte cell-lines, and
its structural and functional properties assessed. This protein migrates
Mr 45,000-70,000 dalton region with a broad singlet or doublet on
SDS-PAGE, specifically binds to C3b and C4b, has an acidic pI around pH 4,
is rich in proline in amino acid analysis, possesses both N-linked and
O-linked oligosaccharides, generates iC3b by acting as a cofactor for
I-mediated C3b cleavage, and does not disassemble the C3 convertases. This
protein therefore shares some common properties characteristic to
complement regulatory proteins, ***CR1*** , H, and C4b-binding protein
( ***C4bp*** ). In addition, the functional profile of this protein is
complementary to that of decay-accelerating factor (DAF) that has been
known to be a protective protein for complement-mediated cell damage. We
named this protein membrane cofactor protein (MCP), and suspect that the
reason DAF and MCP are widely distributed on human peripheral blood cells
relates to their synergistic activity profile such that complement
activation on autologous tissue is inhibited.

L9 ANSWER 32 OF 46 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 90180924 MEDLINE
DOCUMENT NUMBER: 90180924
TITLE: Molecular mapping of the HLA-linked complement genes and
the RCA linkage group.
AUTHOR: Campbell R D; Dunham I; Sargent C A
CORPORATE SOURCE: MRC Immunochemistry Unit, Department of Biochemistry,
University of Oxford, UK..
SOURCE: EXPERIMENTAL AND CLINICAL IMMUNOGENETICS, (1988) 5 (2-3)
81-98. Ref: 113
Journal code: AOK. ISSN: 0254-9670.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
AB Phenotypic genetics have established linkage of the genes encoding
proteins involved in the activation of the complement component C3. C2,
factor B and C4, three of the structural components of the classical and
alternative pathway C3 convertases, are encoded by genes which have been
mapped to the class III region of the major histocompatibility complex
(MHC) on human chromosome 6. The regulatory proteins factor H,
***C4BP*** , ***CR1*** , CR2 and DAF, which are involved in the
control of C3 convertase activity, are encoded by closely linked genes,
termed the regulators of complement activation (RCA) linkage group, that
have been mapped to human chromosome 1. cDNA clones for all these proteins
have been isolated, and this has made it possible to investigate the
organization and structure of the MHC class III genes and the genes in the
RCA linkage group. This short review summarizes some of the main features
which have emerged from recent cloning work.

L9 ANSWER 33 OF 46 MEDLINE
ACCESSION NUMBER: 90009070 MEDLINE
DOCUMENT NUMBER: 90009070
TITLE: C3 receptors on macrophages.
AUTHOR: Law S K
CORPORATE SOURCE: Department of Biochemistry, University of Oxford, UK..
SOURCE: JOURNAL OF CELL SCIENCE. SUPPLEMENT, (1988) 9 67-97. Ref: 187
Journal code: HNG. ISSN: 0269-3518.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199001
AB The complement receptors on macrophage are responsible for their binding and ingestion of opsonized targets. The two established receptors are ***CR1*** , which recognizes C3b, and CR3, which recognizes iC3b, the natural product of C3b from cleavage by the complement control protein factor I and its cofactors. ***CR1*** belongs to a group of proteins that contain a structural element characterized by its size of 60-65 amino acids, and four conservatively positioned cysteines, which engage in a self-contained 1-3, 2-4 disulphide arrangement. This structural unit is called SCR (short consensus repeat) and is found in the complement proteins C1r, C1s, C2, factor B, factor H, ***C4BP*** , DAF, MCP and CR2, each of which interacts with some cleavage products of C3 and/or C4. ***CR1*** has 30 SCR units accounting for its entire extracellular structure. It has a transmembrane segment and a small cytoplasmic domain. CR3 is a heterodimer containing an alpha and beta subunit held together by non-covalent forces. The beta subunit is also found in the two leukocyte antigens, LFA-1 and p150,95, which have alpha subunits distinct from that of CR3. The beta subunit contains 56 cysteine residues, 42 of which lie in a span of 256 residues immediately adjacent to the transmembrane segment. It shares extensive sequence homology with subunits of membrane protein complexes that bind fibronectin and vitronectin, implicating that they all belong to an extended set of surface adhesion molecules not restricted to the immune system. p150,95 is also expressed on macrophages and it has iC3b binding activity. It also shares some functional properties with CR3 as an adhesion surface molecule.

L9 ANSWER 34 OF 46 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 87196375 MEDLINE
DOCUMENT NUMBER: 87196375
TITLE: Expansion of the complement receptor gene family. Identification in the mouse of two new genes related to the ***CR1*** and CR2 gene family.
AUTHOR: Aegerter-Shaw M; Cole J L; Klickstein L B; Wong W W; Fearon D T; Lalley P A; Weis J H
CONTRACT NUMBER: AI-23401 (NIAID)
AI-22833 (NIAID)
AI 07323-01 (NIAID)
+
SOURCE: JOURNAL OF IMMUNOLOGY, (1987 May 15) 138 (10) 3488-94.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
OTHER SOURCE: GENBANK-M16179
ENTRY MONTH: 198708
AB Human cDNA probes encoding the C3b/C4b complement receptor, ***CR1*** , have been used to identify, in the mouse, two new genes which are related to ***CR1*** but which appear to encode a different protein product. These new mouse genes, arbitrarily designated mouse genes X and Y, hybridize specifically to three different cDNA probes derived from human ***CR1*** . The degree of hybridization homology between the mouse X and Y genes suggests they are very closely related to one another; however, the chromosomal localization of the mouse X gene to chromosome 8 and the mouse Y gene to chromosome 1 indicates they are distinct gene sequences. The mRNA species detected with the X and/or Y (X/Y) sequences are approximately 2000 bases in length, but vary in both quantity and size depending upon the tissue analyzed. DNA sequence analysis of a cDNA specific for the X and Y sequences indicates the mature protein(s) will contain the 60 amino acid consensus repeat characteristic of a group of other proteins including ***CR1*** , the C3d receptor (CR2), H, C4 binding protein ( ***C4bp*** ), the interleukin 2 (Il 2) receptor and others. The identity of the mouse X and Y genes, and the function of the proteins which they encode, is not known; however, the small size of the mRNA and the tissue specific expression suggests they do not encode mouse ***CR1*** or CR2 but instead encode a related protein (or proteins) which is expressed in a wide variety of mouse tissues.

L9 ANSWER 35 OF 46 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 87191030 MEDLINE
DOCUMENT NUMBER: 87191030
TITLE: The superfamily of C3b/C4b-binding proteins.
AUTHOR: Kristensen T; D'Eustachio P; Ogata R T; Chung L P; Reid K B; Tack B F
CONTRACT NUMBER: AI 19222 (NIAID)
AI 22214 (NIAID)
GM 29831 (NIGMS)
SOURCE: FEDERATION PROCEEDINGS, (1987 May 15) 46 (7) 2463-9. Ref: 67
Journal code: EUV. ISSN: 0014-9446.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198708
AB The determination of primary structures by amino acid and nucleotide sequencing for the C3b-and/or C4b-binding proteins H, ***C4BP*** , ***CR1*** , B, and C2 has revealed the presence of a common structural element. This element is approximately 60 amino acids long and is repeated in a tandem fashion, commencing at the amino-terminal end of each molecule. Two other complement components, C1r and C1s, have two of these repeating units in the carboxy-terminal region of their noncatalytic A chains. Three noncomplement proteins, beta 2-glycoprotein I (beta 2I), the interleukin 2 receptor (IL 2 receptor), and the b chain of factor XIII, have 4, 2 and 10 of these repeating units, respectively. These proteins obviously belong to the above family, although there is no evidence that they interact with C3b and/or C4b. Human haptoglobin and rat leukocyte common antigen also contain two and three repeating units, respectively, which have more limited homology with the repetitive regions in this family. All available data indicate that multiple gene duplications and exon shuffling have been important features in the divergence of this family of proteins with the 60-amino-acid repeat.

L9 ANSWER 36 OF 46 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1987:615904 CAPLUS
DOCUMENT NUMBER: 107:215904
TITLE: New alleles of C4-binding protein and factor H and further linkage data in the regulator of complement activation (RCA) gene cluster in man
AUTHOR(S): Rodriguez de Cordoba, S.; Rubinstein, P.
CORPORATE SOURCE: Lindsley F. Kimball Res. Inst., New York Blood Cent., New York, NY, 10021, USA
SOURCE: Immunogenetics (1987), 25(4), 267-8
CODEN: IMNGBK; ISSN: 0093-7711
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By isoelec. focusing, a 3rd allele, ***C4BP*** *3, was detected for human complement C4-binding protein ( ***C4BP*** ). Also, in addn. to the 3 genetic variants of factor H, 2 new FH alleles, FH*4 and FH*5, were identified. The exclusive assocn. of the ***C4BP*** *2 allele with C3bR*B haplotypes seems to indicate that the genes coding for ***C4BP*** and ***CR1*** may be in extermely close vicinity.

L9 ANSWER 37 OF 46 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 87252916 MEDLINE
DOCUMENT NUMBER: 87252916
TITLE: Decay-accelerating factor. Genetic polymorphism and linkage to the RCA (regulator of complement activation) gene cluster in humans.
AUTHOR: Rey-Campos J; Rubinstein P; Rodriguez de Cordoba S
CONTRACT NUMBER: DK 19631-11 (NIDDK)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1987 Jul 1) 166 (1) 246-52.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198710
AB We have investigated the genetic relationships between the human decay-accelerating factor (DAF) and a group of complement components including the C3b/C4b receptor ( ***CR1*** ), C4-binding protein ( ***C4bp*** ), and factor H (H), to which DAF is structurally and functionally related. ***CR1*** , ***C4bp*** , and H were previously demonstrated to be encoded by a cluster of closely linked genes, which we have designated regulator of complement activation (RCA). Southern blot analysis of genomic DNA using a DAF cDNA probe unraveled the existence of restriction fragment length polymorphism (RFLP) for both Bam HI and Hind III restriction endonucleases. Segregation analysis of these polymorphic fragments in families informative for the segregation of alleles at the ***CR1*** , ***C4BP*** , and H loci (RCA-haplotypes), demonstrated that, in humans, the gene encoding DAF is located within the RCA gene cluster. No recombinants between DAF and ***C4BP*** / ***CR1*** were encountered in 32 informative meioses. In addition, in two individuals showing recombination between the ***CR1*** / ***C4BP*** and H loci, DAF segregated with the ***CR1*** / ***C4BP*** segment. Thus, the DAF gene maps closer to the ***CR1*** / ***C4BP*** loci than to the H gene, from which it can be separated by genetic recombination.

L9 ANSWER 38 OF 46 BIOSIS COPYRIGHT 1999 BIOSIS
ACCESSION NUMBER: 1988:61486 BIOSIS
DOCUMENT NUMBER: BR34:28182
TITLE: ORGANIZATION OF THE GENES ENCODING ***CR1*** CR2 DAF AND ***C4BP*** IN THE RCA LOCUS ON HUMAN CHROMOSOME ONE.
AUTHOR(S): CARROLL M C; ALICOT E A; KATZMAN P; KLICKSTEIN L B; FEARON D T
CORPORATE SOURCE: DEP. PEDIATR., HARV. MED. SCH., BOSTON, MASS., USA.
SOURCE: XIITH INTERNATIONAL COMPLEMENT WORKSHOP, CHAMONIX, FRANCE, SEPTEMBER 18-21, 1987. COMPLEMENT, (1987) 4 (3-4), 141.
CODEN: CMPLDF. ISSN: 0253-5076.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L9 ANSWER 39 OF 46 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 86183329 MEDLINE
DOCUMENT NUMBER: 86183329
TITLE: The molecular genetics of components of complement.
AUTHOR: Campbell R D; Carroll M C; Porter R R
SOURCE: ADVANCES IN IMMUNOLOGY, (1986) 38

203-44. Ref: 217
Journal code: 2N9. ISSN: 0065-2776.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198607
AB Rapid progress has been made in establishing linkages and in chromosome allocation of the genes of some 9 complement components. In the MHC, C2, Factor B, and two C4 or C4 related genes have been placed in some detail in both man and mouse. The gene coding for the cytochrome P-450 21-hydroxylase has been shown to be duplicated and immediately 3' to the two C4 genes, though it appears to be functionally and structurally unrelated to the complement components. Thus six genes have been mapped to this region where particular haplotypes are associated with increased susceptibility to a number of diseases, some of which are autoimmune in character. The complete gene structure of Factor B has been solved in man and rapid progress is being made with the C2 and C4 genes. The structural basis of the polymorphisms of these genes is being established. In C4, the polymorphism is exceptionally complex with varying numbers of loci and probably more than 50 allotypes occurring in man. A structural basis has also been found for the big differences in the biological activity of some of the C4 allotypes in man. Apart from the genes in the MHC, linkage has been found between the genes coding for ***C4bp*** , ***CR1*** , and Factor H. Remarkably there are sequence homologies between these proteins and C2 and Factor B, probably related to the ability to bind to one or other of the structurally similar proteins C3b and C4b. The complete cDNA sequences of C3 and C4 in mouse and man have given much information on the many posttranslational modifications of these proteins. A partial structure has been obtained for the C3 gene and the homology shown between C3, C4, C5, alpha 2-macroglobulin, and pregnancy zone protein. Although the amount of detailed information in the molecular genetics of complement components is accumulating rapidly, there appears to be a reasonable prospect that linkages and homologies will classify the data into a comprehensible form.

L9 ANSWER 40 OF 46 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 86188123 MEDLINE
DOCUMENT NUMBER: 86188123
TITLE: Partial characterization of human complement factor H by protein and cDNA sequencing: homology with other complement and non-complement proteins.
AUTHOR: Ripoche J; Day A J; Willis A C; Belt K T; Campbell R D; Sim R B
SOURCE: BIOSCIENCE REPORTS, (1986 Jan) 6 (1) 65-72.
Journal code: A6D. ISSN: 0144-8463.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198608
AB Factor H, a control protein of the human complement system, is closely related in functional activity to two other complement control proteins, C4b-binding protein ( ***C4bp*** ) and complement receptor type 1 ( ***CR1*** ). ***C4bp*** is known to have an unusual primary structure consisting of eight homologous units each about 60 amino acids long. Such units also occur in the N-terminal regions of the complement proteins C2 and factor B, and in the non-complement serum glycoprotein beta 2I. Amino acid sequencing, and sequencing of a factor H cDNA clone, show that factor H also contains internal repeating units, and is homologous to the proteins listed above.

L9 ANSWER 41 OF 46 MEDLINE DUPLICATE 19
ACCESSION NUMBER: 85290843 MEDLINE
DOCUMENT NUMBER: 85290843
TITLE: Purification and functional analysis of the polymorphic variants of the C3b/C4b receptor ( ***CR1*** ) and comparison with H, C4b-binding protein ( ***C4bp*** ), and decay accelerating factor (DAF).
AUTHOR: Seya T; Holers V M; Atkinson J P
CONTRACT NUMBER: 5 R01-A119642
SOURCE: JOURNAL OF IMMUNOLOGY, (1985 Oct) 135 (4) 2661-7.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 198512
AB Four ***CR1*** variants have been found in the normal population and are designated ***CR1*** -A (190,000 daltons), ***CR1*** -B (220,000 daltons), ***CR1*** -C (160,000 daltons), and ***CR1*** -D (250,000 daltons). In the present study, we first developed an improved chromatographic purification scheme for ***CR1*** that does not employ a C3b affinity step. ***CR1*** variants (A, B, and C) were then isolated, and their individual functional activity was assessed. Each possessed similar co-factor activity for I-mediated cleavage of C3(H2O), as well as for the inhibitory activity for fluid phase C3 convertases. These results indicate that, despite relatively large Mr differences, in the purified state these three ***CR1*** variants have similar functional activities. The functional activity of ***CR1*** was also compared with ***C4bp*** , H, and decay accelerating factor (DAF) in fluid phase assays designed to assess the inhibition of the C3 convertases and co-factor activity. On a molar basis, ***CR1*** had approximately the same inhibitory activity as ***C4bp*** for the classical pathway convertase, and had the same as H for the alternative pathway convertase. These results indicate that ***CR1*** encompasses the functional capabilities of both proteins. They also raise a number of interesting genetic and structural questions in regard to these complement regulatory proteins, because ***C4bp*** is thought to have multiple C4b binding domains, whereas H is reported to bind one C3b. DAF was an approximately fourfold better inhibitor of the alternative pathway convertase than ***CR1*** or H, but was a fourfold less efficient inhibitor of the classical pathway convertase than ***CR1*** or ***C4bp*** . The effective inhibitory capacity of DAF in these fluid phase assay systems suggests that the DAF substrate specificity is for the convertases. Fluid phase ***CR1*** was twofold less efficient than H in serving as a co-factor for the first cleavage of fluid phase C3b, and hardly mediated the second cleavage. These data are in contrast to the co-factor activity of ***CR1*** on a cell membrane, and provide additional evidence for the local environment being a critical modulator of the function of proteins that regulate the activation of C3.

L9 ANSWER 42 OF 46 MEDLINE DUPLICATE 20
ACCESSION NUMBER: 86130416 MEDLINE
DOCUMENT NUMBER: 86130416
TITLE: Large-scale isolation of complement receptor type 1 ( ***CR1*** ) from human erythrocytes. Proteolytic fragmentation studies.
AUTHOR: Sim R B
SOURCE: BIOCHEMICAL JOURNAL, (1985 Dec 15) 232 (3) 883-9.
Journal code: 9YO. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198605
AB A large-scale procedure for the isolation of complement receptor type 1 ( ***CR1*** , the C3b receptor) from human erythrocytes is described. Two of the four known phenotypes of ***CR1*** are detectable in the isolated material. Amino acid and hexosamine analysis of the A phenotype (Mr 240 000) indicates a polypeptide chain length of about 2030 amino acids and a carbohydrate content of 8%. Both N- and O-linked sugars appear to be present. Trypsin digestion of isolated ***CR1*** shows that it is degraded rapidly and extensively, and no stable products of Mr greater than 25000 are found. The ability of the receptor to bind to solid-phase ligand is destroyed after a single cleavage by trypsin. The capacity of the receptor to act as a cofactor for Factor I-mediated cleavage of soluble C3b is, however, only gradually decreased by proteolysis, and 30% of this activity remains after extensive degradation. The same pattern of loss of binding to solid-phase ligand, with partial retention of interaction with soluble ligand, is also characteristic of the complement proteins Factor H and ***C4bp*** , which are functionally related to ***CR1*** .

L9 ANSWER 43 OF 46 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 85116735 EMBASE
DOCUMENT NUMBER: 1985116735
TITLE: Functional analysis of allelic variants of ***CR1*** and comparison to H, ***C4bp*** and DAF.
AUTHOR: Seya T.; Atkinson J.P.
CORPORATE SOURCE: HHMI at Washington University School of Medicine, St. Louis, MO 63110, United States
SOURCE: Federation Proceedings, (1985) 44/4 (No. 3373).
CODEN: FEPRA7
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English

L9 ANSWER 44 OF 46 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 84214789 MEDLINE
DOCUMENT NUMBER: 84214789
TITLE: Control of the function of substrate-bound C4b-C3b by the complement receptor ***Cr1*** .
AUTHOR: Medof M E; Nussenzweig V
CONTRACT NUMBER: AI-08499 (NIAID)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1984 Jun 1) 159 (6) 1669-85.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198409
AB The complement fragments C3b and C4b are the main ligands for the membrane receptor ***CR1*** . We showed elsewhere that ***CR1*** functions as an essential cofactor for the factor I-mediated enzymatic breakdown of membrane-bound C3b (*C3b) into C3c and * C3dg . One of the main findings of the present paper is that ***CR1*** also promotes the degradation of bound C4b (*C4b) into C4c and *C4d. On a weight basis, the cofactor activity of ***CR1*** in the cleavage of *C4b present on the cell intermediate EAC14 is 10(3)-fold greater than that of the serum cofactor C4-binding protein ( ***C4bp*** ). An additional finding is that the effect of ***CR1*** on either *C3b or *C4b is modulated by the presence of the other ligand in its vicinity; that is, *C4b degradation by ***CR1*** plus I is enhanced by neighboring *C3b and vice versa. For example, upon uptake of optimal amounts of *C3b onto EAC142 and the assembly of the C3-convertase EAC1423 , the activity of ***CR1*** in generating C4c is enhanced 5-10 times further. Conversely, when the number of *C3b molecules on EAC1423 is relatively small (or when EAC1423 has been converted by I plus H into EAC1423i ), the presence of neighboring *C4b enhances the conversion of *C3b (or *iC3b) into C3c plus * C3dg . The enhancing effect of *C3b on the cleavage of *C4b by I is observed only if the cofactor of this reaction is ***CR1*** . Indeed, the activity

of I
or I plus ***C4bp*** on *C4b is significantly inhibited when *C3b is
fixed and the main product of the reaction is * iC4b . Taken together,
these findings suggest that degradation of *C4b will be more effective
when enough C3b molecules are fixed nearby, thus facilitating the
interaction of *C4b*3b clusters with ***CR1*** -bearing cells, and that
under physiological conditions, *C4b activity can be efficiently
controlled by ***CR1*** .

L9 ANSWER 45 OF 46 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 85101648 MEDLINE
DOCUMENT NUMBER: 85101648
TITLE: Protection of the classical and alternative complement pathway C3 convertases, stabilized by nephritic factors, from decay by the human C3b receptor.
AUTHOR: Fischer E; Kazatchkine M D; Mecarelli-Halbwachs L
SOURCE: EUROPEAN JOURNAL OF IMMUNOLOGY, (1984 Dec) 14 (12) 1111-4.
Journal code: EN5. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198505
AB Formation and function of the classical (C4b,2a) and alternative (C3b,Bb)
complement pathway C3 convertases are regulated by the intrinsic lability
of the enzymes, extrinsic decay by ***C4bp*** and H, cleavage of C4b
and C3b by I, and by the inhibitory action of the C3b receptor molecule (
***CR1*** ). Binding of C4 nephritic factor (C4Nef) to C4b and of C3
nephritic factor (C3Nef) to C3b stabilizes the C3 convertases and bypasses
inactivation by ***C4bp*** , H and/or I. In the present study, binding
of C4Nef to the classical C3 convertase was found to prevent decay of
C4b,2a by inputs of ***CR1*** that were at least 15 times the amount
of ***CR1*** which inactivated 50% unstabilized classical pathway C3
convertase sites in 2.5 min. ***CR1*** could however inhibit lysis of
C4b,2a(C4Nef)-bearing cells in a dose-dependent manner. The latter
inhibitory effect was directed at the interaction of C5 with the C5
convertase, most likely at C5 binding to cell-bound C3b. In an analogous
manner to C4Nef in the classical pathway, stabilization of alternative
pathway C3b,Bb convertase sites by C3Nef resulted in a relative protection
of C3 convertase sites from decay by ***CR1*** . Thus, C4Nef and C3Nef
can bypass all mechanisms susceptible to regulate function of the
classical and alternative pathway C3 convertases. Because ***CR1*** is
essential for degradation of C3b bound to immune complexes in whole blood,
stabilization of C4b,2a and C3b,Bb by C4Nef and C3Nef may alter in vivo
processing of immune complexes in patients with nephritic factors.

L9 ANSWER 46 OF 46 MEDLINE DUPLICATE 23
ACCESSION NUMBER: 83162382 MEDLINE
DOCUMENT NUMBER: 83162382
TITLE: Functional properties of membrane-associated complement
receptor ***CR1*** .
AUTHOR: Iida K; Nussenzweig V
CONTRACT NUMBER: AI 08499 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (1983 Apr) 130 (4) 1876-80.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198307
AB It was previously shown that membrane receptors for C3b ( ***CR1*** )
purified from human erythrocytes were powerful inhibitors of the
complement cascade and that they encompass the regulatory functions of the
serum proteins beta 1H (H) and C4-binding protein ( ***C4bp*** ). In the
present report we study the functional properties of membrane-associated
***CR1*** . When tonsil lymphocytes, which contain between 30 and 60% of
***CR1*** -bearing B cells, are incubated with the red cell complement
intermediate EAC14oxy2lim or EAC14oxy23lim, they inhibit both C42 and C423
in a dose-dependent manner. These effects are mediated by
membrane-associated molecules. Indeed, mild trypsinization of the
lymphocytes abolishes their activity, and formaldehyde-fixed cells are as
effective as viable cells. The inhibitory effects are in part mediated by
***CR1*** . The lymphocyte activities are reversed about 60% if
monoclonal antibodies to ***CR1*** or fluid phase C3b are present in
the incubation medium. Moreover, upon addition of C3b-inactivator (I),
lymphocytes release C3c fragments from EAC14oxy23b. The release of C3c was
also abolished by antibodies to ***CR1*** . These results support the
idea that ***CR1*** , as well as other molecules from the lymphocyte
membrane, can function as inhibitor(s) of complement activation in their
vicinity.

=> d l10 ibib abs 1-8

L10 ANSWER 1 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:267203 CAPLUS
DOCUMENT NUMBER: 126:250213
TITLE: Recombinant heteromultimeric C4 binding protein fusion
proteins and their use for vaccines, immunotherapy and
diagnosis
INVENTOR(S): Klatzmann, David; Cohen, Jacques
PATENT ASSIGNEE(S): Universite de Reims Champagne Ardennes, Fr.;
Universite Pierre et Marie Curie Paris VI
SOURCE: Fr. Demande, 36 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 2736916 | A1 | 19970124 | FR 95-8901 | 19950721 |
| FR 2736916 | B1 | 19970919 | | |
| WO 9704109 | A1 | 19970206 | WO 96-FR1132 | 19960718 |

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

| | | | | |
|---|---|---|---|---|
| CA 2227030 | AA | 19970206 | CA 96-2227030 | 19960718 |
| EP 842282 | A1 | 19980520 | EP 96-926424 | 19960718 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: FR 95-8901 19950721
WO 96-FR1132 19960718
AB Disclosed are recombinant multimeric proteins comprising at least (a)
fusion protein A contg. C4 binding protein ( ***C4BP*** ) .alpha. chain
C-terminal residues 124-549 and a heterologous protein and (b) fusion
protein B contg. ***C4BP*** .beta. chain C-terminal residues 120-235
and a heterologous protein, the proteins A and B binding to each other
through the C-terminal domains to form the multimeric protein.
Recombinant cells producing the multimeric proteins as well as use of the
heteromultimers or cells for fetal-maternal alloimmunization, for therapy
or prophylaxis of infections, for therapy of autoimmune diseases, for
immunotherapy and for diagnosis are also disclosed. Thus, anti-Rh(D)
scFv- ***C4BP*** and CD43 fragment- ***C4BP*** fusion proteins were
produced with CHO cells. The heteromultimeric protein formed agglutinated
Rh+ ***erythrocytes*** .

L10 ANSWER 2 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:607743 CAPLUS
DOCUMENT NUMBER: 125:245269
TITLE: Identification of three physically and functionally distinct binding sites for C3b in human ***complement*** factor H by deletion mutagenesis
AUTHOR(S): Sharma, Ajay K.; Pangburn, Michael K.
CORPORATE SOURCE: Department Biochemistry, University Texas Health
Science Center, Tyler, TX, 75710-2003, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1996), 93(20), 10996-11001
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human ***complement*** factor H controls spontaneous activation of
***complement*** in plasma and appears to play a role in distinguishing
host cells from activators of the alternative pathway of
***complement*** . In both mice and humans, the protein is composed of
20 homologous short consensus repeat (SCR) domains. The size of the
protein suggests that portions of the structure outside the known C3b
binding site (SCR 1-4) possess a significant biol. role. We have
expressed the full-length cDNA of factor H in the baculovirus system and
have shown that recombinant protein to be fully active. Mutants of this
full-length protein have now been prepd., purified, and examd. for
cofactor activity and binding to C3b and heparin. The results demonstrate
(i) that factor H has at least three sites that bind C3b, (ii) that one of
these sites is located in SCR domains 1-4, as has been shown by others,
(iii) that a second site exists in the domain 6-10 region, (i.v.) that a
third site resides in the SCR 16-20 region, and (v) that two heparin
binding sites exist in factor H, one near SCR 13 and another in the SCR
6-10 region. Functional assays demonstrated that only the first C3b site
located in SCR 1-4 expresses factor I cofactor activity. Mutant proteins
lacking any one of the three C3b binding sites exhibited 6- to 8-fold
redns. in affinity for C3b on sheep ***erythrocytes*** , indicating
that all three sites contribute to the control of ***complement***
activation on ***erythrocytes*** . The identification of multiple
functionally distinct sites on factor H clarifies many of the heretofore
unexplainable behaviors of this protein, including the heterogeneous
binding of factor H to surface-bound C3b, the effects of trypsin cleavage,
and the differential control of ***complement*** activation on
activators and nonactivators of the alternative pathway of
***complement*** .

L10 ANSWER 3 OF 8 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1994:280266 CAPLUS
DOCUMENT NUMBER: 120:280266
TITLE: Delivery of proteins by intermembrane transfer for preaccommodation of xenogeneic organ transplants and
other purposes
INVENTOR(S): Byrne, Guerard W.; Kooyman, David Lee; Logan, John
Steele
PATENT ASSIGNEE(S): DNX Biotherapeutics, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9406903 | A1 | 19940331 | WO 93-US8889 | 19930922 |

W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| EP 662125 | A1 | 19950712 | EP 93-922259 | 19930922 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC NL, PT, SE

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|---|---|---|---|---|
| JP 08501451 | T2 | 19960220 | JP 93-508379 | 19930922 |
| AU 671158 | B2 | 19960815 | AU 93-51325 | 19930922 |
| FI 9501325 | A | 19950509 | FI 95-1325 | 19950321 |
| NO 9501074 | A | 19950519 | NO 95-1074 | 19950321 |

PRIORITY APPLN. INFO.: US 92-948521 19920922
WO 93-US8889 19930922
AB GPI-linked proteins are transferred, esp. in vivo, from vertebrate carrier
cells to cells of a target vertebrate tissue. For example, for purposes
of xenogeneic transplantation, cells bearing ***complement*** inhibition factor(s) specific for the recipient species, e.g., genetically
engineered red blood cells, are incubated with transplantable cells

of a
second, discordant donor species until transfer of the factor(s) occurs.
The transfer may occur in vivo or in vitro, and the factor-bearing cells
may be normal cells of the recipient species, or genetically engineered
cells of the donor species which express a gene encoding a ***complement*** inhibition factor(s) of the recipient species, e.g.,
DAF, CD59, or others. The method is particularly useful in modifying pig
organs (kidney, heart, etc.) for xenotransplantation into humans.

L10 ANSWER 4 OF 8 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 92017905 MEDLINE
DOCUMENT NUMBER: 92017905
TITLE: Preferential inactivation of the C5 convertase of the alternative ***complement*** pathway by factor I and
membrane cofactor protein (MCP).
AUTHOR: Seya T; Okada M; Matsumoto M; Hong K S; Kinoshita T;
Atkinson J P
CORPORATE SOURCE: Department of Immunology, Center for Adult Diseases Osaka,
Japan.
SOURCE: MOLECULAR IMMUNOLOGY, (1991 Oct) 28 (10) 1137-47.
Journal code: NG1. ISSN: 0161-5890.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199201
AB Human C3b bound to the ghost of sheep ***erythrocytes*** (E*) via
activation of the alternative ***complement*** pathway (E*AC3b)
consists of four major constituents on SDS-PAGE of 350, 260, 210 and 180
kDa. 350 kDa C3b is a dimeric form of C3b in which the alpha' chain of one
C3b binds covalently to that of the other C3b. This complex is presumed to
serve as a core for the alternative pathway C5 convertase. The other C3b
populations are monomers complexed with membrane proteins or sugars. Using
E*AC3b (C3b labeled) as a substrate, we have investigated functional
properties of membrane cofactor protein (MCP), which is an integral
membrane protein with C3b-binding and factor I-dependent cofactor
activities. In conjunction with factor I, MCP was found to degrade the
protein-bound C3b preferentially including the 350 kDa dimer. There was a
similar but lesser tendency of this selective cleavage of C3b-dimer by
***CR1*** but not by factor H or ***C4bp*** . In contrast to
***CR1*** and factor H, detergent solubilization of EAC3b was required
for MCP to fully express its cofactor activity for this selective
degradation of C3b. We next separated the C3b dimer from the monomers and
assessed their ability to assemble the alternative C5 convertase. The C3b
dimer but not the monomers expressed C5 convertase activity following the
addition of factors B and D, C5 and Ni2+. Kinetic analysis of the
degradation of the C3b dimer by MCP and factor I suggested that only one
C3b was efficiently converted to C3bi and this occurred concomitant with a
decrease in C5 convertase activity. These results suggest that MCP has the
ability to more efficiently interact with protein-bound C3b and that this
may relate as well to its preferential ability to irreversibly inactivate
the C5 convertase.

L10 ANSWER 5 OF 8 SCISEARCH COPYRIGHT 1999 ISI (R)
ACCESSION NUMBER: 91:397906 SCISEARCH
THE GENUINE ARTICLE: FW027
TITLE: REGULATORY SYSTEM OF GUINEA-PIG ***COMPLEMENT*** C3B -
TESTS FOR COMPATIBILITY OF GUINEA-PIG FACTOR-H AND
FACTOR-I WITH HUMAN-FACTORS
AUTHOR: SEYA T (Reprint); OKADA M; HAZEKI K; NAGASAWA S
CORPORATE SOURCE: CTR ADULT DIS, DEPT IMMUNOL, HIGASHINARI KU, OSAKA 537,
JAPAN (Reprint); UNIV TOKYO, FAC PHARMACEUT SCI, BUNKYO
KU, TOKYO 113, JAPAN; HOKKAIDO UNIV, FAC PHARMACEUT SCI,
KITA KU, SAPPORO, HOKKAIDO 060, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: MOLECULAR IMMUNOLOGY, (1991) Vol. 28, No. 4-5, pp. 375-382
.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 43
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB Two proteins that are involved in cleavage of methylamine-treated C3 of
guinea-pig origin (C3(MA)gp) have been isolated from guinea-pig serum.
One of them functioned as a cofactor of human factor I (Ihu) for cleavage
of C3(MA)gp and its molecular size was 150 kDa. The other was
functionally pure and able to cleave C3(MA)gp together with human factor H
(Hhu). They appear to be analogous to human factors H and I in the
guinea-pig and will be referred to as Hgp and Igp.
Methylamine-treated human C3 [C3(MA)hu] was not a compatible substrate
for Hgp or Igp: little cleavage of C3(MA)hu was observed if human factor
H (Hhu) or I was substituted with the guinea-pig counterpart. C3(MA)gp,
on the other hand, served as a substrate, though less efficiently, for Hhu
and Ihu. Human C4b-binding protein ( ***C4bp*** ) and membrane cofactor
protein (MCP) as well as Hhu could participate in cleavage of C3(MA)gp by
Igp or Ihu. In these assays, C3(MA)gp was degraded again less efficiently
than C3(MA)hu. Interestingly, human C3b/C4b receptor ( ***CR1*** )
mediated factor I-dependent cleavage of C3(MA)hu and C3(MA)gp to a similar
extent regardless the sources of factor I. These results suggest that
factor I-dependent C3b regulatory system is species-specific except in the
case of ***CR1*** , which may function as a cofactor irrespective of
species.

L10 ANSWER 6 OF 8 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 86130416 MEDLINE
DOCUMENT NUMBER: 86130416
TITLE: Large-scale isolation of ***complement*** receptor type
1 ( ***CR1*** ) from human ***erythrocytes*** .
Proteolytic fragmentation studies.
AUTHOR: Sim R B
SOURCE: BIOCHEMICAL JOURNAL, (1985 Dec 15) 232 (3) 883-9.
Journal code: 9YO. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198605
AB A large-scale procedure for the isolation of ***complement*** receptor
type 1 ( ***CR1*** , the C3b receptor) from human ***erythrocytes***
is described. Two of the four known phenotypes of ***CR1*** are
detectable in the isolated material. Amino acid and hexosamine analysis of
the A phenotype (Mr 240 000) indicates a polypeptide chain length of about
2030 amino acids and a carbohydrate content of 8%. Both N- and O-linked
sugars appear to be present. Trypsin digestion of isolated ***CR1***
shows that it is degraded rapidly and extensively, and no stable products
of Mr greater than 25000 are found. The ability of the receptor to bind to
solid-phase ligand is destroyed after a single cleavage by trypsin. The
capacity of the receptor to act as a cofactor for Factor I-mediated
cleavage of soluble C3b is, however, only gradually decreased by
proteolysis, and 30% of this activity remains after extensive degradation.
The same pattern of loss of binding to solid-phase ligand, with partial
retention of interaction with soluble ligand, is also characteristic of
the ***complement*** proteins Factor H and ***C4bp*** , which are
functionally related to ***CR1*** .

L10 ANSWER 7 OF 8 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 84214789 MEDLINE
DOCUMENT NUMBER: 84214789
TITLE: Control of the function of substrate-bound C4b-C3b by the
***complement*** receptor ***Cr1*** .
AUTHOR: Medof M E; Nussenzweig V
CONTRACT NUMBER: AI-08499 (NIAID)
SOURCE: JOURNAL OF EXPERIMENTAL MEDICINE, (1984 Jun 1) 159 (6)
1669-85.
Journal code: I2V. ISSN: 0022-1007.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198409
AB The ***complement*** fragments C3b and C4b are the main ligands for
the membrane receptor ***CR1*** . We showed elsewhere that ***CR1***
functions as an essential cofactor for the factor I-mediated enzymatic
breakdown of membrane-bound C3b (*C3b) into C3c and * C3dg . One of the
main findings of the present paper is that ***CR1*** also promotes the
degradation of bound C4b (*C4b) into C4c and *C4d. On a weight basis, the
cofactor activity of ***CR1*** in the cleavage of *C4b present on the
cell intermediate EAC14 is 10(3)-fold greater than that of the serum
cofactor C4-binding protein ( ***C4bp*** ). An additional finding is
that the effect of ***CR1*** on either *C3b or *C4b is modulated by
the presence of the other ligand in its vicinity; that is, *C4b
degradation by ***CR1*** plus I is enhanced by neighboring *C3b and
vice versa. For example, upon uptake of optimal amounts of *C3b onto
EAC142 and the assembly of the C3-convertase EAC1423 , the activity of
***CR1*** in generating C4c is enhanced 5-10 times further. Conversely,
when the number of *C3b molecules on EAC1423 is relatively small (or when
EAC1423 has been converted by I plus H into EAC1423i ), the presence of
neighboring *C4b enhances the conversion of *C3b (or *iC3b) into C3c plus
* C3dg . The enhancing effect of *C3b on the cleavage of *C4b by I is
observed only if the cofactor of this reaction is ***CR1*** . Indeed,
the activity of I or I plus ***C4bp*** on *C4b is significantly
inhibited when *C3b is fixed and the main product of the reaction is *
iC4b . Taken together, these findings suggest that degradation of *C4b
will be more effective when enough C3b molecules are fixed nearby, thus
facilitating the interaction of *C4b*3b clusters with ***CR1***
-bearing cells, and that under physiological conditions, *C4b activity can
be efficiently controlled by ***CR1*** .

L10 ANSWER 8 OF 8 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 83162382 MEDLINE
DOCUMENT NUMBER: 83162382
TITLE: Functional properties of membrane-associated ***complement*** receptor ***CR1*** .
AUTHOR: Iida K; Nussenzweig V
CONTRACT NUMBER: AI 08499 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (1983 Apr) 130 (4) 1876-80.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198307
AB It was previously shown that membrane receptors for C3b ( ***CR1*** )
purified from human ***erythrocytes*** were powerful inhibitors of the
***complement*** cascade and that they encompass the regulatory
functions of the serum proteins beta 1H (H) and C4-binding protein (
***C4bp*** ). In the present report we study the functional properties of
membrane-associated ***CR1*** . When tonsil lymphocytes, which contain
between 30 and 60% of ***CR1*** -bearing B cells, are incubated with
the red cell ***complement*** intermediate EAC14oxy2lim or
EAC14oxy23lim, they inhibit both C42 and C423 in a dose-dependent manner.
These effects are mediated by membrane-associated molecules. Indeed, mild
trypsinization of the lymphocytes abolishes their activity, and
formaldehyde-fixed cells are as effective as viable cells. The

inhibitory
effects are in part mediated by ***CR1*** . The lymphocyte activities
are reversed about 60% if monoclonal antibodies to ***CR1*** or fluid
phase C3b are present in the incubation medium. Moreover, upon addition of
C3b-inactivator (I), lymphocytes release C3c fragments from EAC14oxy23b.
The release of C3c was also abolished by antibodies to ***CR1*** .
These results support the idea that ***CR1*** , as well as other
molecules from the lymphocyte membrane, can function as inhibitor(s) of
***complement*** activation in their vicinity.

=> d l11 ibib abs 1-2

L11 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:267203 CAPLUS
DOCUMENT NUMBER: 126:250213
TITLE: Recombinant heteromultimeric C4 binding protein fusion
proteins and their use for vaccines, immunotherapy and
diagnosis
INVENTOR(S): Klatzmann, David; Cohen, Jacques
PATENT ASSIGNEE(S): Universite de Reims Champagne Ardennes, Fr.;
Universite Pierre et Marie Curie Paris VI
SOURCE: Fr. Demande, 36 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 2736916 | A1 | 19970124 | FR 95-8901 | 19950721 |
| FR 2736916 | B1 | 19970919 | | |
| WO 9704109 | A1 | 19970206 | WO 96-FR1132 | 19960718 |

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

| | | | | |
|---|---|---|---|---|
| CA 2227030 | AA | 19970206 | CA 96-2227030 | 19960718 |
| EP 842282 | A1 | 19980520 | EP 96-926424 | 19960718 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

PRIORITY APPLN. INFO.: FR 95-8901 19950721
WO 96-FR1132 19960718
AB Disclosed are recombinant multimeric proteins comprising at least (a)
fusion protein A contg. C4 binding protein ( ***C4BP*** ) .alpha. chain
C-terminal residues 124-549 and a heterologous protein and (b) fusion
protein B contg. ***C4BP*** .beta. chain C-terminal residues 120-235
and a heterologous protein, the proteins A and B binding to each other
through the C-terminal domains to form the multimeric protein.
Recombinant cells producing the multimeric proteins as well as use of the
heteromultimers or cells for fetal-maternal alloimmunization, for therapy
or prophylaxis of infections, for therapy of autoimmune diseases, for
immunotherapy and for diagnosis are also disclosed. Thus, ***anti*** -
***Rh*** (D) scFv- ***C4BP*** and CD43 fragment- ***C4BP*** fusion
proteins were produced with CHO cells. The heteromultimeric protein
formed agglutinated Rh+ erythrocytes.

L11 ANSWER 2 OF 2 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998022791 MEDLINE
DOCUMENT NUMBER: 98022791
TITLE: A recombinant human scFv ***anti*** - ***Rh*** (D)
antibody with multiple valences using a C-terminal fragment
of C4-binding protein.
AUTHOR: Libyh M T; Goossens D; Oudin S; Gupta N; Dervillez X;
Juszczak G; Cornillet P; Bougy F; Reveil B; Philbert F; Tabary T; Klatzmann D; Rouger P; Cohen J H
CORPORATE SOURCE: Laboratoire d'Immunologie, UFR Medecine, Pole Biomolecules
URCA, Reims, France.
SOURCE: BLOOD, (1997 Nov 15) 90 (10) 3978-83.
Journal code: A8G. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer
Journals
ENTRY MONTH: 199802
ENTRY WEEK: 19980204
AB Monomeric recombinant molecules prove generally unsatisfactory for in vivo
use. Most biological systems are indeed multivalent either structurally,
associating different chains, or functionally, when cross-linked by their
ligands. Mimicking natural molecules for immune intervention implies the
need for multimerizing systems to create multivalent molecules capable of
interfering with physiological processing. A multivalent ***anti*** -
***Rh*** (D) recombinant protein has been designed by reconstructing the
antibody binding site of a human monoclonal ***anti*** - ***Rh*** (D)
antibody as a single chain Fv mini antibody, then multimerizing it by
inserting at its C-terminal end the C-terminal part of the C4 binding
protein ( ***C4bp*** ) alpha chain, which is responsible for the octamer
multimerization of that molecule. This soluble multivalent recombinant
molecule was functional, bound red blood cells (RBCs), agglutinated them,
and did not activate complement. This demonstration model opens the way
for future in vivo use of multivalent molecules associating antibody
valences and other functional molecules for cell targeting, imaging, or
removal of cells such as Rh(D)-positive RBCs for preventing Rh alloimmunization.

=> d l12 ibib abs 1-4

L12 ANSWER 1 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:252939 CAPLUS
DOCUMENT NUMBER: 124:286566
TITLE: Human skeletal myoblasts spontaneously activate allogeneic ***complement*** but are resistant to killing
AUTHOR(S): Gasque, Philippe; Morgan, B. Paul; Legoedec, Jocelyne;
Chan, Philippe; Fontaine, Marc
CORPORATE SOURCE: Dep. Med. Biochem., Univ. Wales Coll. Med., Cardiff,
UK
SOURCE: J. Immunol. (1996), 156(9), 3402-11
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ***complement*** (C) system has previously been implicated in
several diseases of muscle. We here report that human myoblasts or
rhabdomyosarcoma cell lines spontaneously activate C through the classical
pathway, causing release of anaphylatoxins and coating of myoblasts with
. opsonic C fragments but without causing cell killing. Survival of
myoblasts is a consequence of the abundant expression of the membrane C
regulatory mols. MCP and CD59, and neutralization of CD59 renders cells
susceptible to C killing. The decay-accelerating factor was expressed at
a very low level. Myoblasts and rhabdomyosarcoma lines also abundantly
express the fluid-phase regulators C1-inhibitor, factor H, C4 binding
protein, ***S*** - ***protein*** , and clusterin and secrete a sol.
form of CD59. Expression of membrane and fluid-phase regulators is
enhanced by either IFN-.gamma. or TNF-.alpha.. Although myoblasts resist
C killing, spontaneous activation of C on these cells may have important
consequences in inflammatory diseases of muscle where the generation of
anaphylactic and opsonic fragments with recruit and activate inflammatory
cells. C activation on myoblasts may also have consequences for the use
of these cells as vehicles for gene delivery. Inhibition of C using sol.
***complement*** receptor 1 (sCR1) efficiently protected myoblasts from
C attack in vitro, and this agent, already being tested in therapy of
several C-mediated diseases, might be of value in inflammatory muscle
disease and in improving the efficiency of gene delivery.

L12 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1996:708713 CAPLUS
DOCUMENT NUMBER: 126:6135
TITLE: ***Complement*** regulatory protein expression by
a human oligodendrocyte cell line: cytokine regulation and comparison with astrocytes
AUTHOR(S): Gasque, P.; Morgan, B. P.
CORPORATE SOURCE: Dep. of Medical Biochemistry, Tenovus Building,
Cardiff, CF4 4XX, UK
SOURCE: Immunology (1996), 89(3), 338-347
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rat oligodendrocytes spontaneously active ***complement*** (C) and
lack the C inhibitor CD59. As a consequence, rat oligodendrocytes are
susceptible to lysis by autologous C in vitro. Expression of C inhibitors
on human oligodendrocytes in vitro and other human glia has yet to be well
characterized. We have previously shown expression at the mRNA level of
the membrane inhibitors CD59, decay-accelerating factor (DAF; CD55) and
membrane cofactor protein (MCP; CD46) in human astrocytes. We here
examine the expression of membrane and secreted C inhibitors by the
oligodendrocyte cell line, HOG. HOG cells abundantly expressed CD59,
assessed at protein and mRNA level, and expressed CAF and MCP, albeit at a
lower level. Expression of all three inhibitors was enhanced by
incubation with interferon-.gamma. or with phorbol ester (PMA).
***Complement*** receptor type 1 ( ***CR1*** ; ***CD35*** ) was
neither expressed constitutively nor induced by cytokines. HOG also
constitutively secreted C1-inhibitor, ***S*** - ***protein*** and
clusterin. Factor H was secreted only after stimulation with cytokines.
C4b binding proteins was expressed at a very low level and was detected
only at the mRNA level by reversed transcriptase-polymerase chain reaction
(Rt-PCR). For comparison, astrocyte expression of CD59, DAF, MCP and
***CR1*** was confirmed at the mRNA and protein levels. HOG did not
activate C spontaneously, as judged by the lack of deposition of C
fragments, and were not lysed by C even after inhibition of CD59 and DAF
using specific monoclonal antibodies.

L12 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:649734 CAPLUS
DOCUMENT NUMBER: 117:249734
TITLE: ***Complement*** activation in the follicular light zone of human lymphoid tissues
AUTHOR(S): Yamakawa, M.; Imai, Y.
CORPORATE SOURCE: Sch. Med., Yamagata Univ., Yamagata 900-23, Japan
SOURCE: Immunology (1992), 76(3), 378-84
CODEN: IMMUAM; ISSN: 0019-2805
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A comparative immunohistochem. study of the distribution pattern of
***complement*** components and regulatory proteins within secondary
lymphoid follicles was performed by the immunoperoxidase technique.
Fifteen lymphoid tissues including appendices, Peyer's patches and tonsils
were analyzed. Sixty secondary lymphoid follicles with evident polarity,
i.e., the distinct coexistence of a light zone, dark zone and mantle zone
in the same lymphoid follicle, were tested with single antibodies. The
light zones were consistently immunostained in a dendritic meshwork
pattern with all antibodies. The immunostaining patterns were classified
into two major groups based on the immunoreactivity of the dark zone. One
immunostaining pattern was characterized by no immunostaining of the dark
zone to the majority of the antigens. The second group was characterized
by a diffusely weak to moderate dendritic meshwork pattern of the dark
zone to some immunostaining for C9 (monoclonal), ***S*** - ***protein*** , and DF-DRC1, and all immunostaining of ***CR1*** (

***CD35*** ), Ber-Mac-DRC ( ***CD35*** ), CR2(CD21), and R4/23. All
four ***complement*** regulatory proteins were localized by immunoelectron microscopy attached to the cell surface of the cells,
including follicular dendritic cells, in the light zone. The data indicate that there is an evident functional difference between the light
zone and the dark zone, and that complete activation of the ***complement*** system occurs only in the light zone.

L12 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1992:52936 CAPLUS
DOCUMENT NUMBER: 116:52936
TITLE: C4 binding protein fusions with therapeutically useful proteins
INVENTOR(S): Pasek, Mark P.; Winkler, Gunther; Liu, Theresa R.
PATENT ASSIGNEE(S): Biogen, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9111461 | A1 | 19910808 | WO 91-US567 | 19910128 |
| W: AU, CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | |
| AU 9173288 | A1 | 19910821 | AU 91-73288 | 19910128 |
| EP 465633 | A1 | 19920115 | EP 91-903951 | 19910128 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE | | | | |
| JP 04506460 | T2 | 19921112 | JP 91-504137 | 19910128 |

PRIORITY APPLN. INFO.: US 90-470888 19900126
WO 91-US567 19910128

AB The ***complement*** C4 binding protein ( ***C4bp*** ) is used in
fusion proteins with therapeutic proteins to ensure targetting of the fusion protein to the blood and to prolong serum half-life. In
particular, the short consensus repeats of the N-terminal region are used.
The primary aim is to provide ***CD4*** antigens for use in the
treatment of AIDS. A cDNA for ***C4bp*** was cloned by polymerase
chain reaction amplification of the mRNA and subloned into the animal
expression vector pJOD-10. When the cloned gene was expressed in COS-7
cells a heptameric ***C4bp*** of the correct conformation but lacking
the ***S*** ***protein*** -binding subunit was produced. Chimeric
genes based upon this cDNA and one encoding sol. ***CD4*** antigen
were constructed and expressed in COS-7 cells. The purified fusion
proteins were shown to form multimers and to bind the glycoprotein gp120
of HIV in vitro. Conditioned medium from producer cells prevented
syncytia formation by HIV-infected cells.

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FILE 'MEDLINE, JAPIO, BIOSIS, SCISEARCH, CAPLUS, EMBASE' ENTERED AT
16:18:32 ON 25 APR 1999
L1 983 S C4BP
L2 106 S L1 AND (CD4 OR CD8 OR CD16 OR CD35 OR CR1)
L3 103 S L2 AND (COAGULATION OR COMPLEMENT)
L4 18 S L3 AND ERYTHROCYTE?
L5 1 S L3 AND C TERMINAL
L6 0 S L2 AND RATIO
L7 6 S L1 AND (ANTI-RH OR ANTI RH)
L8 4 S L3 AND S PROTEIN?
L9 46 DUP REM L2 (60 DUPLICATES REMOVED)
L10 8 DUP REM L4 (10 DUPLICATES REMOVED)
L11 2 DUP REM L7 (4 DUPLICATES REMOVED)
L12 4 DUP REM L8 (0 DUPLICATES REMOVED)

=> d l5 ibib abs

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1999 ACS
ACCESSION NUMBER: 1997:267203 CAPLUS
DOCUMENT NUMBER: 126:250213
TITLE: Recombinant heteromultimeric C4 binding protein fusion proteins and their use for vaccines, immunotherapy and diagnosis
INVENTOR(S): Klatzmann, David; Cohen, Jacques
PATENT ASSIGNEE(S): Universite de Reims Champagne Ardennes, Fr.;
Universite Pierre et Marie Curie Paris VI
SOURCE: Fr. Demande, 36 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| FR 2736916 | A1 | 19970124 | FR 95-8901 | 19950721 |
| FR 2736916 | B1 | 19970919 | | |
| WO 9704109 | A1 | 19970206 | WO 96-FR1132 | 19960718 |
| W: CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2227030 | AA | 19970206 | CA 96-2227030 | 19960718 |
| EP 842282 | A1 | 19980520 | EP 96-926424 | 19960718 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |

PRIORITY APPLN. INFO.: FR 95-8901 19950721
WO 96-FR1132 19960718

AB Disclosed are recombinant multimeric proteins comprising at least (a)
fusion protein A contg. C4 binding protein ( ***C4BP*** ) .alpha. chain
***C*** - ***terminal*** residues 124-549 and a heterologous protein
and (b) fusion protein B contg. ***C4BP*** .beta. chain ***C*** -
***terminal*** residues 120-235 and a heterologous protein, the proteins
A and B binding to each other through the ***C*** - ***terminal***
domains to form the multimeric protein. Recombinant cells producing the
multimeric proteins as well as use of the heteromultimers or cells for
fetal-maternal alloimmunization, for therapy or prophylaxis of infections,
for therapy of autoimmune diseases, for immunotherapy and for diagnosis
are also disclosed. Thus, anti-Rh(D) scFv- ***C4BP*** and CD43
fragment- ***C4BP*** fusion proteins were produced with CHO cells. The
heteromultimeric protein formed agglutinated Rh+ erythrocytes.

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